COVID-19 Evidence Support Team
EVIDENCE SEARCH REPORT

Review Question: What is the epidemiology of the omicron variant and its impact on healthcare?
Context: Split from variant ongoing search/review
Review Code: EOC211220v011 ESR Complete Date: March 11, 2022

Librarian Notes & Comments

Hello,

This search report includes the following content pertaining to omicron epidemiology:

1) Grey literature results from the past week.
2) A separate list of journal articles and preprints that were NOT captured by Ovid auto-alerts.
   (n=##)
3) A complete list of references that had previously been delivered via Ovid (Embase & MEDLINE) daily auto-alerts – emailed to stakeholders. (n=##)

We will continue to provide these updates each Friday of the week.

Sincerely,
Lukas & Mark

CC: Brianna

Search Results: Guidelines, Summaries & Other Grey Literature

Disclaimer
This information is provided as a service by the Saskatchewan Health Authority and University of Saskatchewan Libraries. Professional librarians conduct searches of the literature. Results are subject to the limitations of the databases and the specificity, breadthness and appropriateness of the search parameters presented by the requester. The Libraries do not represent in any matter that retrieved citations are complete, accurate or otherwise to be relied upon. The search results are only valid as of the date and time at which the search is conducted. The Libraries do not accept responsibility for any loss or damage arising from the use of, or reliance on, search results.
Health Canada

BCCDC

Manitoba Government

Public Health Ontario | Ministry of Health

ECDC

UK Health Security Agency | GOV.UK

Imperial College London
- Coronavirus infections remain high while Omicron ‘s stealth variant’ rises – REACT. 10 March 2022. [https://www.imperial.ac.uk/news/234517/coronavirus-infections-remain-high-while-omicron/](https://www.imperial.ac.uk/news/234517/coronavirus-infections-remain-high-while-omicron/)

COVID-19 Critical Intelligence Unit (Australia)

WHO

CIDRAP
• Third vaccine dose boosts Omicron protection, with some waning. 3 March 2022.  
  https://www.cidrap.umn.edu/news-perspective/2022/03/third-vaccine-dose-boosts-omicron-protection-some-waning

• Asia’s Omicron surges soar as US adds technology to WHO-led push 3 March 2022.  
  https://www.cidrap.umn.edu/news-perspective/2022/03/asias-omicron-surges-soar-us-adds-technology-who-led-push

CBC News

• Half of Manitobans may have contracted Omicron: Toronto researcher. 10 March 2022.  

The Guardian

• One-third of all US child Covid deaths occurred during Omicron surge. 11 March 2022.  

• What is the Deltacron variant of Covid and where has it been found? 11 March 2022.  
  https://www.theguardian.com/world/2022/mar/11/what-is-deltacron-covid-variant-uk

Reuters

• Variant that combines Delta and Omicron identified; dogs sniff out virus with high accuracy. 9 March 2022.  

Search Results: Journal Articles (includes preprints) – HANDSEARCHED

Sorted by newest-oldest.


Background A rapid increase in incidence of the SARS-CoV-2 Omicron variant occurred in France in December 2021, while the Delta variant was prevailing since July 2021. We aimed to determine whether the risk of a severe hospital event following symptomatic SARS-CoV-2 infection differs for Omicron versus Delta. Methods We conducted a retrospective cohort study to compare severe hospital events (admission to intensive care unit or death) between Omicron and Delta symptomatic cases matched according to week of virological diagnosis and age. The analysis was adjusted for age, sex, vaccination status, presence of comorbidities and region of residence, using Cox proportional hazards model. Findings Between 06/12/2021-28/01/2022, 184 364 cases were included, of which 931 had a severe hospital event (822 Delta, 109 Omicron). The risk of severe event was lower among Omicron versus Delta cases; the difference in severity between the two variants decreased with age (aHR=0.11 95%CI: 0.07-0.17 among 40-64 years, aHR=0.51 95%CI: 0.26-1.01 among 80+ years). The risk of severe event increased with the presence of comorbidities (for very-high-risk comorbidity, aHR=4.18 95%CI: 2.88-6.06 among 40-64 years and in males (aHR=2.29 95%CI: 1.83-2.86 among 40-64 years) and was higher in unvaccinated compared to primo-vaccinated (aHR=6.90 95%CI: 5.26-9.05 among 40-64 years). A booster dose reduced the risk of severe hospital event in 80+ years infected with Omicron (aHR=0.27; 95%CI: 0.11-0.65). Interpretation This study confirms the lower severity of Omicron compared to Delta. However, the difference in disease severity is less marked in the elderly. Competing Interest Statement The authors have declared no competing interest. Funding Statement The study was performed as part of routine work at Public Health France. Author Declarations I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained. Yes The details of the IRB/oversight body that provided approval or exemption for the research described are given below: Ethics committee of Public Health France waived ethical approval for this work confirm that all necessary patient/participant
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consent has been obtained and the appropriate institutional forms have been archived, and that any patient/participant/sample identifiers included were not known to anyone (e.g., hospital staff, patients or participants themselves) outside the research group so cannot be used to identify individuals. Yes I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance). Yes I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable. Yes While all data used in this analysis were pseudonymised, the individual-level nature of the data used risks individuals being identified, or being able to self-identify, if it is released publicly. Requests for access to the underlying source data should be directed to Public Health France and will be granted in accordance with the GDPR and French Law.

URL: http://medrxiv.org/content/early/2022/03/07/2022.02.02.22269952.abstract
DOI: 10.1101/2022.02.02.22269952

2. Bruhn C. What’s next for omicron?: The research on the new virus variant is in full swing. Deutsche Apotheker Zeitung. 2022;162(4).

DOI:


BACKGROUND: The SARS-CoV-2 Omicron variant BA.2 sublineage has increased rapidly in Europe and Asia since January 2022. Here, we report the epidemiological and genomic analysis of a large single source BA.2 outbreak in a housing estate. METHODS: We analyzed the epidemiological information of a community outbreak of BA.2 (STY outbreak). We performed whole viral genome sequencing using the Oxford Nanopore MinION device. We calculated the doubling time of the outbreak within a housing estate. RESULTS: The STY outbreak involved a total of 768 individuals as of 5th February 2022, including 432 residents, visitors or staff (56.3%) from a single housing estate (KC Estate). The outbreak at the KC Estate has a short doubling time of 1.28 days (95% confidence interval: 0.560-1.935). The outbreak was promptly controlled with the lockdown of 3 buildings within the housing estate. Whole genome sequencing was performed for 133 patients in the STY outbreak, including 106 residents of the KC Estate. All 133 sequences from the STY outbreak belonged to the BA.2 sublineage, and phylogenetic analysis showed that these sequences cluster together. All individuals in the STY cluster had the unique mutation C12525T. CONCLUSIONS: Our study highlights the exceptionally high transmissibility of the Omicron variant BA.2 sublineage in Hong Kong where stringent measures are implemented as part of the elimination strategy. Continual genomic surveillance is crucial in monitoring the emergence of epidemiologically important Omicron sub-variants.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35271728
DOI: 10.1093/cid/ciac203


Multiple SARS-CoV-2 variants have successively, or concomitantly spread worldwide since summer 2020. A few co-infections with different variants were reported and genetic recombinations, common among coronaviruses, were reported or suspected based on co-detection of signature mutations of different variants in a given genome. Here we report three infections in southern France with a Delta 21J/AY.4-Omicron 21K/BA.1 “Deltamicron” recombinant. The hybrid genome harbors signature mutations of the
two lineages, supported by a mean sequencing depth of 1,163-1,421 reads and mean nucleotide diversity of 0.1-0.6%. It is composed of the near full-length spike gene (from codons 156-179) of an Omicron 21K/BA.1 variant in a Delta 21J/AY.4 lineage backbone. It is similar to those reported for 15 other patients sampled since January 2022 in Europe. Importantly, we cultured an isolate of this recombinant and sequenced its genome. It was observed by scanning electron microscopy. As it is misidentified with current variant screening qPCR, we designed and implemented for routine diagnosis a specific duplex qPCR. Finally, structural analysis of the recombinant spike suggested its hybrid content could optimize viral binding to the host cell membrane. These findings prompt further studies of the virological, epidemiological, and clinical features of this recombinant.

Competing Interest Statement Didier Raoult has a conflict of interest as having been a consultant for Hitachi High-Technologies Corporation, Tokyo, Japan from 2018 to 2020. He is a scientific board member of Eurofins company and a founder of a microbial culture company (Culture Top). All other authors have no conflicts of interest to declare. Funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript. Funding Statement This work was supported by the French Government under the Investments for the Future program managed by the National Agency for Research (ANR), Mediterranean-Infection 10-IAHU-03; by Region Provence Alpes Cote d'Azur and European funding FEDER PRIMMI (Fonds European de Developpement Regional-Plateformes de Recherche et d&#039;Innovation Mutualisees Mediterranean Infection), FEDER PA 0000320 PRIMMI; by Hitachi High-Technologies Corporation, Tokyo, Japan; and by the French consortium on surveillance and research on infections with emerging pathogens via microbial genomics (consortium releatif a la surveillance et a la recherche sur les infections a pathogenes EMERgents via la GE Nomique microbienne EMERGEN; https://www.santepubliquefrance.fr/dossiers/coronavirus-sarscov2/covid-19/consortium-emergen). Author Declarations I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained. Yes The details of the IRB/oversight body that provided approval or exemption for the research described are given below: This study has been approved by the ethics committee of the University Hospital Institute Mediterranean Infection (No. 2022-001). Access to the patients biological and registry data issued from the hospital information system was approved by the data protection committee of Assistance Publique-Hopitaux de Marseille (APHM) and was recorded in the European General Data Protection Regulation registry under number RGPD/APHM 2019-73.I confirm that all necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived, and that any patient/participant/sample identifiers included were not known to anyone (e.g., hospital staff, patients or participants themselves) outside the research group so cannot be used to identify individuals. Yes I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance). Yes I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable. Yes The dataset generated and analyzed during the current study is available in the GISAID database (https://www.gisaid.org/).

URL: http://medrxiv.org/content/early/2022/03/08/2022.03.03.22271812.abstract
DOI: 10.1101/2022.03.03.22271812


We report evidence of Delta/Omicron SARS-CoV-2 co-infections during the fifth wave of COVID-19 pandemics in France for 7 immunocompetent and epidemiologically unrelated patients. These co-infections were detected by PCR assays targeting SARS-CoV-2 S-gene mutations K417N and L452R and confirmed by whole genome sequencing which allowed the proportion estimation of each subpopulation. For 2 patients, the analyses of longitudinal samples collected 7 to 11 days apart showed that Delta or Omicron...
can outcompete the other variant during dual infection. Competing Interest Statement The authors have declared no competing interest. Funding Statement This study did not receive any funding. Author Declarations I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained. Yes The details of the IRB/oversight body that provided approval or exemption for the research described are given below: This study was based on national surveillance data. Informed consent was obtained from all patients. The study was approved by the review committee of the University Hospital of Clermont-Ferrand, France 2022/CE06. I confirm that all necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived, and that any patient/participant/sample identifiers included were not known to anyone (e.g., hospital staff, patients or participants themselves) outside the research group so cannot be used to identify individuals. Yes I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance). Yes I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable. Yes All data produced in the present work are contained in the manuscript.

URL: http://medrxiv.org/content/early/2022/03/03/2022.03.02.22271694.abstract
DOI: 10.1101/2022.03.02.22271694


Objectives To describe the severity of maternal infection when the Omicron SARS-CoV-2 variant was dominant (15/12/21-14/01/22) and compare outcomes among groups with different vaccination status. Design Prospective cohort study Setting UK consultant-led maternity units Participants Pregnant women hospitalised with a positive SARS-CoV-2 PCR test up to 7 days prior to admission and/or during admission up to 2 days after giving birth. Main outcome measures Symptomatic or asymptomatic infection. Vaccination status. Severity of maternal infection (moderate or severe infection according to modified WHO criteria). Mode of birth and perinatal outcomes. Results Out of 1561 women admitted to hospital with SARS-CoV-2 infection, 449 (28.8%) were symptomatic. Among symptomatic women admitted, 86 (19.2%) had moderate to severe infection; 51 (11.4%) had pneumonia on imaging, 62 (14.3%) received respiratory support, and 19 (4.2%) were admitted to the intensive care unit (ICU). Three women died (0.7%). Vaccination status was known for 383 symptomatic women (85.3%) women; 249 (65.0%) were unvaccinated, 45 (11.7%) had received one vaccine dose, 76 (19.8%) had received two doses and 13 (3.4%) had received three doses. 59/249 (23.7%) unvaccinated women had moderate to severe infection, compared to 10/45 (22.2%) who had one dose, 9/76 (11.8%) who had two doses and 0/13 (0%) who had three doses. Among the 19 symptomatic women admitted to ICU, 14 (73.7%) were unvaccinated, 3 (15.8%) had received one dose, 1 (5.3%) had received two doses, 0 (0%) had received 3 doses and 1 (5.3%) had unknown vaccination status. Conclusion The risk of severe respiratory disease amongst unvaccinated pregnant women admitted with symptomatic SARS-CoV-2 infection during the Omicron dominance period was comparable to that observed during the period the wildtype variant was dominant. Most women with severe disease were unvaccinated. Vaccine coverage amongst pregnant women admitted with SARS-CoV-2 was low compared to the overall pregnancy population and very low compared to the general population. Ongoing action to prioritise and advocate for vaccine uptake in pregnancy is essential.

SUMMARY BOX What is already known on this topic In non-pregnant adults, growing evidence indicates a lower risk of severe respiratory disease with the Omicron SARS-CoV-2 Variant of Concern (VOC). Pregnant women admitted during the periods in which the Alpha and Delta VOC were dominant were at increased risk of moderate to severe SARS-CoV-2 infection compared to the period when the original wildtype infection was dominant. Most women admitted to hospital with symptomatic SARS-CoV-2 infection have been unvaccinated. What this study adds One in four women who had received no vaccine...
or a single dose had moderate to severe infection, compared with one in eight women who had received
two doses and no women who had received three doses. The proportional rate of moderate to severe
infection in unvaccinated pregnant women during the Omicron dominance period is similar to the rate
observed during the wildtype dominance period. One in eight symptomatic admitted pregnant women
needed respiratory support during the period when Omicron was dominant.

**Competing Interest Statement**

All authors have completed the ICMJE uniform disclosure form [www.icmje.org/coi_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: MK, MQ, PB, POB, JJK received grants from the NIHR in relation to the submitted work. HE participated in this work as an academic visitor to the NPEU with funding from The Norwegian Research Council, grant no 320181, and travel grant from the Nordic Federation of Societies of Obstetrics and Gynecology Research fund, grant no 6302. KB, NV, RR, NS, CG have no conflicts of interest to declare. EM is Trustee and President of RCOG. POB is Vice President of RCOG and Co-Chair of the RCOG Vaccine Committee. No other relationships or activities that could appear to have influenced the submitted work.


**Funding Statement**
The study was funded by the National Institute for Health Research HS&amp;DR Programme (project number 11/46/12). MK is an NIHR Senior Investigator. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

**Author Declarations**

I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained. Yes

The details of the IRB/oversight body that provided approval or exemption for the research described are given below: The HRA NRES Committee East Midlands Nottingham 1 gave ethical approval for this work (Reference Number 12/EM/0365). I confirm that all necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived, and that any patient/participant/sample identifiers included were not known to anyone (e.g., hospital staff, patients or participants themselves) outside the research group so cannot be used to identify individuals. Yes

I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance). Yes

I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable. Yes

Data Sharing Data cannot be shared publicly because of confidentiality issues and potential identifiability of sensitive data as identified within the Research Ethics Committee application/approval. Requests to access the data can be made by contacting the National Perinatal Epidemiology Unit data access committee via general@npeu.ox.ac.uk.

**URL:** [http://medrxiv.org/content/early/2022/03/09/2022.03.07.22271699.abstract](http://medrxiv.org/content/early/2022/03/09/2022.03.07.22271699.abstract)

**DOI:** 10.1101/2022.03.07.22271699


**DOI:** 10.1016/j.tmaid.2022.102262


Wastewater monitoring of SARS-CoV-2 allows for early detection and monitoring of COVID-19 burden in communities and can track specific variants of concern. Targeted assays enabled relative proportions of SARS-CoV-2 Omicron and Delta variants to be determined across 30 municipalities covering &amp;gt;75% of the province of Alberta (pop. 4.5M) in Canada, from November 2021 to January 2022. Larger cities like
Calgary and Edmonton exhibited a more rapid emergence of Omicron relative to smaller and more remote municipalities. Notable exceptions were Banff, a small international resort town, and Fort McMurray, a more remote northern city with a large fly-in worker population. The integrated wastewater signal revealed that the Omicron variant represented close to 100% of SARS-CoV-2 burden prior to the observed increase in newly diagnosed clinical cases throughout Alberta, which peaked two weeks later. These findings demonstrate that wastewater monitoring offers early and reliable population-level results for establishing the extent and spread of emerging pathogens including SARS-CoV-2 variants. Competing Interest Statement The authors have declared no competing interest. Funding Statement This work was supported by the Japan Agency for Medical Research and Development (grant numbers JP20fk0108535). K.I. received funding JSPS KAKENHI (21H03490). C.P. was supported by the World-leading Innovative and Smart Education Program (1801) from the Ministry of Education, Culture, Sports, Science, and Technology, Japan. H.N. received funding from Health and Labor Sciences Research Grants (20CA2024, 20HA2007, and 21HB1002); the Japan Agency for Medical Research and Development (JP20fk0108140); JSPS KAKENHI (21H03198) and the Japan Science and Technology Agency (JST) SICORP program (JPMJSC20U3 and JPMJSC2105). The funders had no role in the study design, data collection and analysis.
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decision to publish, or preparation of the manuscript. Author Declarations: I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained. Yes I confirm that all necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived, and that any patient/participant/sample identifiers included were not known to anyone (e.g., hospital staff, patients or participants themselves) outside the research group so cannot be used to identify individuals. Yes I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance). Yes I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable. Yes All data produced in the present work are contained in the manuscript.

URL: http://medrxiv.org/content/early/2022/03/04/2022.03.02.22271767.abstract
DOI: 10.1101/2022.03.02.22271767

The new SARS-CoV-2 B.1.1.529 Omicron variant has spread rapidly throughout the world, including in countries such as Norway with 90% primary vaccination and increasing booster vaccination coverage. To enable alignment of infection control measures with the risk posed by the new variant and avoid excessive strain on health systems, estimates of the transmissibility of the Omicron variant are needed. We assessed the secondary attack rate of Omicron and B.1.617.2 Delta variants in households in Norway.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35254379
DOI: 10.1001/jama.2022.3780


URL: https://www.ncbi.nlm.nih.gov/pubmed/35246640
DOI: 10.1038/d41586-022-00632-3

12. Ngonghala CN, Taboe HB, Gumel AB. Dynamics of the Delta and Omicron variants of SARS-CoV-2 in the United States: the battle of supremacy in the presence of vaccination, mask usage and antiviral treatment. 2022. DOI: 10.21203/rs.3.rs-1420446/v1
The effectiveness of control interventions against COVID-19 is threatened by the emergence of SARS-CoV-2 variants of concern. We present a mathematical model for studying the transmission dynamics of two of these variants (Delta and Omicron) in the United States, in the presence of vaccination, treatment of individuals with clinical symptoms of the disease and the use of face masks. Using current daily case data for COVID-19, we showed that the predominant Omicron variant can be eliminated if current control measures are maintained at their baseline levels. Vaccine-derived herd immunity can be achieved (so that the pandemic will be eliminated) if at least 68% of the population is fully-vaccinated. We showed that elimination is feasible by June 2022 if current baseline level of full vaccination coverage is increased by about 20%. The prospect of pandemic elimination is significantly improved if vaccination is combined with a face mask strategy that prioritizes moderately effective and high-quality masks. Having a high percentage of the populace wearing the moderately-effective surgical mask is more beneficial to the community than having low percentage of the populace wearing the highly-effective N95 masks. We showed that waning natural and vaccine-derived immunity (if considered individually) offer marginal impact on disease burden, except for the case when they wane at a much faster rate (e.g., within three months), in comparison to the baseline (estimated to be within 9 months to a year). Treatment of symptomatic individuals has marginal effect in reducing daily cases of SARS-CoV-2, in comparison to the
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Introduction Globally, there have been more than 404 million cases of SARS-CoV-2, with 5.8 million confirmed deaths, as of February 2022. South Africa has experienced four waves of SARS-CoV-2 transmission, with the second, third, and fourth waves being driven by the Beta, Delta, and Omicron variants, respectively. A key question with the emergence of new variants is the extent to which they are able to reinfect those who have had a prior natural infection. Rationale We developed two approaches to monitor routine epidemiological surveillance data to examine whether SARS-CoV-2 reinfection risk has changed through time in South Africa, in the context of the emergence of the Beta (B.1.351), Delta (B.1.617.2), and Omicron (B.1.1.529) variants. We analyze line list data on positive tests for SARS-CoV-2 with specimen receipt dates between 04 March 2020 and 31 January 2022, collected through South Africa’s National Notifiable Medical Conditions Surveillance System. Individuals having sequential positive tests at least 90 days apart were considered to have suspected reinfections. Our routine monitoring of reinfection risk included comparison of reinfection rates to the expectation under a null model (approach 1) and estimation of the time-varying hazards of infection and reinfection throughout the epidemic (approach 2) based on model-based reconstruction of the susceptible populations eligible for primary and second infections. Results 105,323 suspected reinfections were identified among 2,942,248 individuals with laboratory-confirmed SARS-CoV-2 who had a positive test result at least 90 days prior to 31 January 2022. The number of reinfections observed through the end of the third wave in September 2021 was consistent with the null model of no change in reinfection risk (approach 1). Although increases in the hazard of primary infection were observed following the introduction of both the Beta and Delta variants, no corresponding increase was observed in the reinfection hazard (approach 2). Contrary to expectation, the estimated hazard ratio for reinfection versus primary infection was lower during waves driven by the Beta and Delta variants than for the first wave (relative hazard ratio for wave 2 versus wave 1: 0.71 (CI95: 0.60–0.85); for wave 3 versus wave 1: 0.54 (CI95: 0.45–0.64)). In contrast, the recent spread of the Omicron variant has been associated with an increase in reinfection hazard coefficient. The estimated hazard ratio for reinfection versus primary infection versus wave 1 was 1.75 (CI95: 1.48–2.10) for the period of Omicron emergence (01 November 2021 to 30 November 2021) and 1.70 (CI95: 1.44–2.04) for wave 4 versus wave 1. Individuals with identified reinfections since 01 November 2021 had experienced primary infections in all three prior waves, and an increase in third infections has been detected since mid-November 2021. Many individuals experiencing third infections had second infections during the third (Delta) wave that ended in September 2021, strongly suggesting that these infections resulted from immune evasion rather than waning immunity. Conclusion Population-level evidence suggests that the Omicron variant is associated with substantial ability to evade immunity from prior infection. In contrast, there is no population-wide epidemiological evidence of immune escape associated with the Beta or Delta variants. This finding has important implications for public health planning, particularly in countries like South Africa with high rates of immunity from prior infection. Further development of methods to track reinfection risk during pathogen emergence, including refinements to assess the impact of waning immunity, account for vaccine-derived protection, and monitor the risk of multiple reinfections will be an important tool for future pandemic preparedness. Competing Interest Statement All authors have completed the ICMJE uniform disclosure form. CC and AvG have received funding from Sanofi Pasteur in the past 36 months. JRCP and KM serve on the Ministerial Advisory Committee on COVID-19 of the South African National Department of Health. The authors have declared no other relationships or activities that could appear to have influenced the submitted work. Funding Statement This work was supported by the South African Department of Science and Innovation and the National Research Foundation and the

URL: DOI: 10.21203/rs.3.rs-1420446/v1

Qassim SH, Chemaitelly H, Ayoub HH, et al. Effects of BA.1/BA.2 subvariant, vaccination, and prior infection on infectiousness of SARS-CoV-2 Omicron infections. medRxiv. 2022;2022.03.02.22271771. DOI: 10.1101/2022.03.02.22271771

BACKGROUND Qatar experienced a large SARS-CoV-2 Omicron (B.1.1.529) wave that started on December 19, 2021 and peaked in mid-January, 2022. We investigated effects of Omicron subvariant (BA.1 and BA.2), previous vaccination, and prior infection on infectiousness of Omicron infections, between December 23, 2021 and February 20, 2022.

METHODS Univariable and multivariable regression analyses were conducted to estimate the association between the RT-qPCR cycle threshold (Ct) value of PCR tests (a proxy for SARS-CoV-2 infectiousness) and each of the Omicron subvariants, mRNA vaccination, prior infection, reason for RT-qPCR testing, calendar week of RT-qPCR testing (to account for phases of the rapidly evolving Omicron wave), and demographic factors. RESULTS Compared to BA.1, BA.2 was associated with 3.53 fewer cycles (95% CI: 3.46–3.60), signifying higher infectiousness. Ct value decreased with time since second and third vaccinations. Ct values were highest for those who received their boosters in the month preceding the RT-qPCR test—0.86 cycles (95% CI: 0.72–1.00) higher than for unvaccinated persons. Ct value was 1.30 (95% CI: 1.20–1.39) cycles higher for those with a prior infection compared to those without prior infection, signifying lower infectiousness. Ct value declined gradually with age. Ct value was lowest for those who were tested because of symptoms and was highest for those who were tested for travel-related purposes. Ct value was lowest during the exponential-growth phase of the Omicron wave and was highest after the wave peaked and was declining. CONCLUSIONS The BA.2 subvariant appears substantially more infectious than the BA.1 subvariant. This may reflect higher viral load and/or longer duration of infection, thereby explaining the rapid expansion of this subvariant in Qatar.
Background Vaccination with COVID-19 mRNA vaccines prevent hospitalization and severe disease caused by wildtype SARS-CoV-2 and several variants, and likely prevented infection when serum neutralizing antibody (NAb) titers were ≥1:160. Preventing infection limits viral replication resulting in mutation, which can lead to the emergence of additional variants. Methods During a longitudinal study to evaluate durability of a three-dose mRNA vaccine regimen (2 primary doses and a booster) using a rapid test that semi-quantitatively measures NAb, the Omicron variant emerged and quickly spread globally. We evaluated NAb levels measured prior to symptomatic breakthrough infection, in groups infected prior to and after the emergence of Omicron. Results During the SARS-CoV-2 Delta variant wave, 93% of breakthrough infections in our study occurred when serum NAb titers were ≥1:80. In contrast, after the emergence of Omicron, study participants with high NAb titers that had received booster vaccine doses became symptomatically infected. NAb titers prior to infection were ≥1:640 in 64% of the Omicron-infected population, ≥1:320 (14%), and ≥1:160 (21%). Discussion These results indicate that high titers of NAb elicted by currently available mRNA vaccines do not protect against infection with the Omicron variant, and that mild to moderate symptomatic infections did occur in a vaccinated and boosted population, although did not require hospitalization. Competing Interest Statement DFL and SS are co-founders of Sapphire, the research division of AXIM Biotechnologies. SS, MGM, and AS-N are employed by AXIM. All other authors have no competing interests to report. Funding Statement This study was funded in part by Sapphire/AXIM Biotechnologies, Inc. (San Diego, CA). The funder had no role in the study design, collection, analysis, and interpretation of data. All authors and co-authors performed the study independent of influence of the funders. Author Declarations confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained. Yes The details of the IRB/oversight body that provided approval or exemption for the research described are given below: Hamad Medical Corporation and Weill Cornell Medicine-Qatar Institutional Review Boards approved this retrospective study with waiver of informed consent. I confirm that all necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived, and that any patient/participant/sample identifiers included were not known to anyone (e.g., hospital staff, patients or participants themselves) outside the research group so cannot be used to identify individuals. Yes I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance). Yes I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable. Yes The dataset of this study is a property of the Qatar Ministry of Public Health that was provided to the researchers through a restricted-access agreement that prevents sharing the dataset with a third party or publicly. Future access to this dataset can be considered through a direct application for data access to Her Excellency the Minister of Public Health (https://www.moph.gov.qa/english/Pages/default.aspx). Aggregate data are available within the manuscript and its Supplementary information.
have been archived, and that any patient/participant/sample identifiers included were not known to anyone (e.g., hospital staff, patients or participants themselves) outside the research group so cannot be used to identify individuals. Yes, I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance). Yes, I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable. Yes, all data produced in the present work are contained in the manuscript and supplementary materials. Additional data not included are available upon reasonable request to the corresponding author.

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DOI: 10.1101/2022.03.03.22270812


We studied a unique case of prolonged viral shedding in an immunocompromised patient that generated a series of SARS-CoV-2 immune escape mutations over a period of seven months. During the persisting SARS-CoV-2 infection, seventeen non-synonymous mutations were observed, thirteen (13/17; 76.5%) of which occurred in the genomic region coding for spike. Fifteen (15/17; 88.2%) of these mutations have already been described in the context of variants of concern and include the prominent immune escape mutations S:E484K, S:D950N, S:P681H, S:N501Y, S:del(9), N:S235F and S:H655Y. Fifty percent of all mutations acquired by the investigated strain (11/22) are found in similar form in the Omicron variant of concern. The study shows the chronology of the evolution of intra-host mutations, which can be seen as the straight mutational response of the virus to specific antibodies and should therefore be given special attention in the rating of immune escape mutations of SARS-CoV-2. Competing Interest Statement The authors have declared no competing interest. Funding Statement We gratefully acknowledge the financial support of the Austrian Research Promotion Agency (FFG), Grant No. 889135. Author Declaration I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained. Yes, The details of the IRB/oversight body that provided approval or exemption for the research described are given below: Ethical approval to use residual routinely taken serum samples for retrospective analyses was obtained by the Ethics Committee of the University Hospital Wuerzburg (no. 20201105_01). I confirm that all necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived, and that any patient/participant/sample identifiers included were not known to anyone (e.g., hospital staff, patients or participants themselves) outside the research group so cannot be used to identify individuals. Yes, I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance). Yes, I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable. Yes, The generated full-genome sequences are available at GISAID EpiCoV (https://gisaid.org/no.EPI_ISL_2106191-21061201). https://gisaid.org/no.EPI_ISL_2106191-21061201

URL: http://medrxiv.org/content/early/2022/03/07/2022.03.04.22271540.abstract
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INTRODUCTION: The coronavirus disease 2019 (COVID-19) first reported in Wuhan, China in December 2019 is a global pandemic that is threatening the health and well-being of people worldwide. To date there have been more than 274 million reported cases and 5.3 million deaths. The omicron variant first documented in the City of Tshwane, Gauteng Province, South Africa on 9 November 2021 led to exponential increases in cases and a sharp rise in hospital admissions. The clinical profile of patients admitted at a large hospital in Tshwane is compared with previous waves. METHODS: 466 hospital COVID-19 admissions since 14 November 2021 were compared to 3962 admissions since 4 May 2020, prior to the omicron outbreak. Ninety-eight patient records at peak bed occupancy during the outbreak were reviewed for primary indication for admission, clinical severity, oxygen supplementation level, vaccination and prior COVID-19 infection. Provincial and city-wide daily cases and reported deaths, hospital admissions and excess deaths data were sourced from the National Institute for Communicable Diseases, the National Department of Health and the South African Medical Research Council. RESULTS: For the omicron and previous waves, deaths and ICU admissions were 4.5% vs 21.3% (p<0.00001), and 1% vs 4.3% (p<0.00001) respectively; length of stay was 4.0 days vs 8.8 days; and mean age was 39 years vs 49.8 years. Admissions in the Omicron wave peaked and declined rapidly with peak bed occupancy at 51% of the highest previous peak during the Delta wave. Sixty-two (63%) patients in COVID-19 wards had incidental COVID-19 following a positive SARS-CoV-2 PCR test. Only one third (36%) had COVID-19 pneumonia, of which 72% had mild to moderate disease. The remaining 28% required high care or ICU admission. Fewer than half (45%) of patients in COVID-19 wards required oxygen supplementation compared to 99.5% in the first wave. The death rate in the face of an exponential increase in cases during the omicron wave at the city and provincial levels shows a decoupling of cases and deaths compared to previous waves, corroborating the clinical findings of decreased severity of disease seen in patients admitted to the Steve Biko Academic Hospital. CONCLUSION: There was decreased severity of COVID-19 disease in the omicron-driven fourth wave in the City of Tshwane, its first global epicentre.

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BACKGROUND: Waning of COVID-19 vaccine protection and emergence of SARS-CoV-2 Omicron (B.1.1.529) variant have expedited efforts to scale up booster vaccination. This study compared protection afforded by booster doses of the BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) vaccines, compared to the primary series of only two doses in Qatar, during a large, rapidly growing Omicron wave. METHOD(S): In a population of 2,232,224 vaccinated persons with at least two doses, two matched, retrospective cohort studies were implemented to investigate effectiveness of booster vaccination against symptomatic SARS-CoV-2 infection and against COVID-19 hospitalization and death, up to January 9, 2022. Association of booster status with infection was estimated using Cox proportional-hazards regression models. RESULT(S): For BNT162b2, cumulative symptomatic infection incidence was 2.9% (95% CI: 2.8-3.1%) in the booster-dose cohort and 5.5% (95% CI: 5.3-5.7%) in the primary-series cohort, after 49 days of follow-up. Adjusted hazard ratio for symptomatic infection was 0.50 (95% CI: 0.47-0.53). Booster effectiveness relative to primary series was 50.1% (95% CI: 47.3-52.8%). For mRNA-1273, cumulative symptomatic infection incidence was 1.9% (95% CI: 1.7-2.2%) in the booster-dose cohort and 3.5% (95% CI: 3.2-3.9%) in the primary-series cohort, after 35 days of follow-up. The adjusted hazard ratio for symptomatic infection was 0.49 (95% CI: 0.43-0.57). Booster effectiveness relative to primary series was 50.8% (95% CI: 43.4-57.3%). There were fewer cases of severe COVID-19 in booster-dose cohorts than in primary-series cohorts, but cases of severe COVID-19 were rare in all cohorts. CONCLUSION(S): mRNA booster
vaccination is associated with modest effectiveness against symptomatic infection with Omicron. The development of a new generation of vaccines targeting a broad range of variants may be warranted. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

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BACKGROUND: Waning of vaccine protection against coronavirus disease 2019 (Covid-19) and the emergence of the omicron (or B.1.1.529) variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have led to expedited efforts to scale up booster vaccination. Protection conferred by booster doses of the BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) vaccines in Qatar, as compared with protection conferred by the two-dose primary series, is unclear. METHODS: We conducted two matched retrospective cohort studies to assess the effectiveness of booster vaccination, as compared with that of a two-dose primary series alone, against symptomatic SARS-CoV-2 infection and Covid-19-related hospitalization and death during a large wave of omicron infections from December 19, 2021, through January 26, 2022. The association of booster status with infection was estimated with the use of Cox proportional-hazards regression models. RESULTS: In a population of 2,239,193 persons who had received at least two doses of BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) vaccine, those who had also received a booster were matched with persons who had not received a booster. Among the BNT162b2-vaccinated persons, the cumulative incidence of symptomatic omicron infection was 2.4% (95% confidence interval [CI], 2.3 to 2.5) in the booster cohort and 4.5% (95% CI, 4.3 to 4.6) in the nonbooster cohort after 35 days of follow-up. Booster effectiveness against symptomatic omicron infection, as compared with that of the primary series, was 49.4% (95% CI, 47.1 to 51.6). Booster effectiveness against Covid-19-related hospitalization and death due to omicron infection, as compared with the primary series, was 76.5% (95% CI, 55.9 to 87.5). BNT162b2 booster effectiveness against symptomatic infection with the delta (or B.1.617.2) variant, as compared with the primary series, was 86.1% (95% CI, 67.3 to 94.1). Among the mRNA-1273-vaccinated persons, the cumulative incidence of symptomatic omicron infection was 1.0% (95% CI, 0.9 to 1.2) in the booster cohort and 1.9% (95% CI, 1.8 to 2.1) in the nonbooster cohort after 35 days; booster effectiveness against symptomatic omicron infection, as compared with the primary series, was 47.3% (95% CI, 40.7 to 53.3). Few severe Covid-19 cases were noted in the mRNA-1273-vaccinated cohorts. CONCLUSIONS: The messenger RNA (mRNA) boosters were highly effective against symptomatic delta infection, but they were less effective against symptomatic omicron infection. However, with both variants, mRNA boosters led to strong protection against Covid-19-related hospitalization and death. (Funded by Weill Cornell Medicine-Qatar and others.).

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The performance of Covid-19 diagnostic tests must continue to be reassessed with new variants of concern. The objective of this study was to describe the discordance in saliva SARS-CoV-2 PCR and nasal rapid antigen test results during the early infectious period. We identified a high-risk occupational case cohort of 30 individuals with daily testing during an Omicron outbreak in December 2021. Based on viral load and transmissions confirmed through epidemiological investigation, most Omicron cases were infectious for several days before being detectable by rapid antigen tests. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license.

On the 26th of November 2021 the World Health Organization (WHO) designated the newly detected B.1.1.529 lineage of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) the Omicron Variant of Concern (VOC). The genome of the Omicron VOC contains more than 50 mutations, many of which have been associated with increased transmissibility, differing disease severity, and potential to evade immune responses developed for previous VOCs such as Alpha and Delta. In the days since the designation of B.1.1.529 as a VOC, infections with the lineage have been reported in countries around the globe and many countries have implemented travel restrictions and increased border controls in response. We putatively detected the Omicron variant in an aircraft wastewater sample from a flight arriving to Darwin, Australia from Johannesburg, South Africa on the 25th of November 2021 via positive results on the CDC N1, CDC N2, and del(69-70) RT-qPCR assays per guidance from the WHO. The Australian Northern Territory Health Department detected one passenger onboard the flight who was infected with SARS-CoV-2, which was determined to be the Omicron VOC by sequencing of a nasopharyngeal swab sample. Subsequent sequencing of the aircraft wastewater sample using the ARTIC V3 protocol with Nanopore and ATOPlex confirmed the presence of the Omicron variant with a consensus genome that clustered with the B.1.1.529 BA.1 sub-lineage. Our detection and confirmation of a single onboard Omicron infection via aircraft wastewater further bolsters the important role that aircraft wastewater can play as an independent and unintrusive surveillance point for infectious diseases, particularly coronavirus disease 2019.

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The SARS-CoV-2 Omicron variant has a growth advantage over the Delta variant because of higher transmissibility, immune evasion or shorter serial interval. Using S gene target failure (SGTF) as indication for Omicron BA.1, we identified 908 SGTF and 1,621 non-SGTF serial intervals in the same period. Within households, the mean serial interval for SGTF cases was 0.2-0.6 days shorter than for non-SGTF cases. This suggests that the growth advantage of Omicron is partly due to a shorter serial interval.

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In 2019, the Canadian Government released a national dementia strategy that identified the need to address the health inequity (e.g., avoidable, unfair, and unjust differences in health outcomes) and improve the human rights of people living with dementia. However, the novel coronavirus disease 2019 (COVID-19) pandemic is having an inequitable impact on people with dementia in terms of mortality and human rights violations. As the new Omicron COVID-19 variant approaches its peak, our commentary highlights the need for urgent action to support people living with dementia and their care partners. More specifically, we argue that reducing COVID-19 inequities requires addressing underlying population-level factors known as the social determinants of health. Health disparities cannot be rectified merely by looking at mortality rates of people with dementia. Thus, we believe that improving the COVID-19 outcomes of people with dementia requires addressing key determinants such as where people live, their social supports, and having equitable access to healthcare services. Drawing on Canadian-based examples, we conclude that COVID-19 policy responses to the pandemic must be informed by evidence-informed
research and collaborative partnerships that embrace the lived experience of diverse people living with dementia and their care partners.

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The B.1.1.529 (Omicron) variant, first detected in November 2021, was responsible for a surge in U.S. infections with SARS-CoV-2, the virus that causes COVID-19, during December 2021-January 2022 (1). To investigate the effectiveness of prevention strategies in household settings, CDC partnered with four U.S. jurisdictions to describe Omicron household transmission during November 2021-February 2022. Persons with sequence-confirmed Omicron infection and their household contacts were interviewed. Omicron transmission occurred in 124 (67.8%) of 183 households. Among 431 household contacts, 227 were classified as having a case of COVID-19 (attack rate [AR] = 52.7%). (dagger) The ARs among household contacts of index patients who had received a COVID-19 booster dose, of fully vaccinated index patients who completed their COVID-19 primary series within the previous 5 months, and of unvaccinated index patients were 42.7% (47 of 110), 43.6% (17 of 39), and 63.9% (69 of 108), respectively. The AR was lower among household contacts of index patients who isolated (41.2%, 99 of 240) compared with those of index patients who did not isolate (67.5%, 112 of 166) (p-value <0.01). Similarly, the AR was lower among household contacts of index patients who never wore a mask at home during their potentially infectious period (39.5%, 88 of 223) compared with those of index patients who ever wore a mask at home (68.9%, 124 of 180) (p-value <0.01). Multicomponent COVID-19 prevention strategies, including up-to-date vaccination, isolation of infected persons, and mask use at home, are critical to reducing Omicron transmission in household settings.

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URL: https://www.ncbi.nlm.nih.gov/pubmed/35189538
DOI: 10.1016/j.ejca.2022.01.010


Background SARS-CoV-2 infection is associated with enhanced disease severity in pregnant women. Despite the potential of COVID-19 vaccines to reduce severe disease, vaccine uptake remained relatively low among pregnant women. Just as coordinated messaging from the CDC and leading obstetrics organizations began to increase vaccine confidence in this vulnerable group, the evolution of SARS-CoV-2 variants of concerns (VOC) including the Omicron VOC raised new concerns about vaccine efficacy, given their ability to escape vaccine-induced neutralizing antibodies. Early data point to a milder disease course following omicron VOC infection in vaccinated individuals. Thus, these data suggest that alternate vaccine induced immunity, beyond neutralization, may continue to attenuate omicron disease, such as antibody-Fc-mediated activity. However, whether vaccine induced antibodies raised in pregnancy continue to bind and leverage Fc-receptors remains unclear. Methods VOC including Omicron receptor binding domain (RBD) or full Spike specific antibody isotype binding titers and FcgammaR binding were analyzed in pregnant women after the full dose regimen of either Pfizer/BioNTech BNT62b2 (n=10) or Moderna mRNA-1273 (n=10) vaccination using a multiplexing Lumine assay. Findings Comparable, albeit reduced, isotype recognition was observed to the Omicron Spike and receptor binding domain (RBD) following both vaccines. Yet, despite the near complete loss of Fc-receptor binding to the Omicron RBD, Fc-receptor binding was
largely preserved to the Omicron Spike. Interpretation Reduced binding titer to the Omicron RBD aligns with observed loss of neutralizing activity. Despite the loss of neutralization, preserved Omicron Spike recognition and Fc-receptor binding potentially continues to attenuate disease severity in pregnant women.

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While children have been largely spared from COVID-19 disease, the emergence of viral variants of concern (VOC) with increased transmissibility, combined with fluctuating mask mandates and school re-openings have led to increased infections and disease among children. Thus, there is an urgent need to roll out COVID-19 vaccines to children of all ages. However, whether children respond equivalently to adults to mRNA vaccines and whether dosing will elicit optimal immunity remains unclear. Given the recent announcement of incomplete immunity induced by the pediatric dose of the BNT162b2 vaccine in young children, here we aimed to deeply profile and compare the vaccine-induced humoral immune response in 6-11 year old children receiving the pediatric (50μg) or adult (100μg) dose of the mRNA-1273 vaccine compared to adults and naturally infected children or children that experienced multi inflammatory syndrome in children (MIS-C) for the first time. Children elicited an IgG dominant vaccine induced immune response, surpassing adults at a matched 100μg dose, but more variable immunity at a 50μg dose. Irrespective of titer, children generated antibodies with enhanced Fc-receptor binding capacity. Moreover, like adults, children generated cross-VOC humoral immunity, marked by a decline of omicron receptor binding domain-binding, but robustly preserved omicron Spike-receptor binding, with robustly preserved Fc-receptor binding capabilities, in a dose dependent manner. These data indicate that while both 50μg and 100μg of mRNA vaccination in children elicits robust cross-VOC antibody responses, 100μg of mRNA in children results in highly preserved omicron-specific functional humoral immunity.

**One-Sentence Summary:** mRNA vaccination elicits robust humoral immune responses to SARS-CoV-2 in children 6-11 years of age.

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Omicron is an emerging SARS-CoV-2 variant, evolved from the Indian delta variant B.1.617.2, which is currently infecting worldwide. The spike glycoprotein, an important molecule in the pathogenesis and transmissions of SARS-CoV-2 variants, especially omicron B.1.1.529, shows 37 mutations distributed over the trimeric protein domains. Notably, fifteen of these mutations reside in the receptor-binding domain of the spike glycoprotein, which may alter transmissibility and infectivity. Additionally, the omicron spike evades neutralization more efficiently than the delta spike. Most of the therapeutic antibodies are ineffective against the omicron variant, and double immunization with BioNTech-Pfizer (BNT162b2) might not adequately protect against severe disease induced by omicron B.1.1.529. So far, no efficient antiviral drugs are available against omicron. The present study identified the promising inhibitors from seaweed’s bioactive compounds to inhibit the omicron variant B.1.1.529. We have also compared the seaweed’s compounds with the standard drugs ceftriaxone and cefuroxime, which were suggested as beneficial antiviral drugs in COVID-19 treatment. Our molecular docking analysis revealed that caffeic acid hexoside (-6.4 kcal/mol; RMSD = 2.382 Å) and phloretin (-6.3 kcal/mol; RMSD = 0.061 Å) from Sargassum wightii (S. wightii) showed the inhibitory effect against the crucial residues ASN417, SER496, TYR501, and HIS505, which are supported for the inviolable omicron and angiotensin-converting enzyme II (ACE2) receptor interaction. Cholestan-3-ol, 2-methylene-,(3beta, 5 alpha) (CMBA) (-6.0 kcal/mol; RMSD = 3.074 Å) from
Corallina officinalis (C. officinalis) manifested the strong inhibitory effect against the omicron RBD mutated residues LEU452 and ALA484, was magnificently observed as the essential residues in Indian delta variant B.1.617.2 previously. The standard drugs (ceftriaxone and cefuroxime) showed no or less inhibitory effect against RBD of omicron B.1.1.529. The present study also emphasized the pharmacological properties of the considered chemical compounds. The results could be used to develop potent seaweed-based antiviral drugs and/or dietary supplements to treat omicron B.1.1529-infected patients.

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DOI: 10.3390/md20020148


URL: https://www.ncbi.nlm.nih.gov/pubmed/35108465
DOI: 10.1056/NEJMp2119682


URL: https://www.ncbi.nlm.nih.gov/pubmed/35229932
DOI: 10.1002/uog.24893


As SARS-CoV-2 has evolved, so has its effects on the pediatric population.1 While early variants typically resulted in lower respiratory infections, the recently identified Omicron variant may exhibit a predilection for the upper airways.2 The relatively smaller upper respiratory tract in children compared to adults has been thought to predispose them to more severe clinical presentations resembling laryngotracheobronchitis, or croup. Caused by viral-induced subglottic airway inflammation, croup is classically characterized by sudden onset "barking cough", inspiratory stridor, and respiratory distress. Endemic coronaviruses have been linked to croup, however only sparse case reports have described croup specifically associated with SARS-CoV-2 and it remains unclear if croup cases constitute a causative relationship or result of co-infection with another virus.3-6 To address this knowledge gap, we performed a retrospective analysis of the incidence and clinical characteristics of croup associated with SARS-CoV-2 infection at a large freestanding children's hospital.

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Background The incidence of SARS-CoV-2 infection, including among those who have received 2 doses of COVID-19 vaccines, increased substantially following the emergence of Omicron in Ontario, Canada. Methods Applying the test-negative study design to linked provincial databases, we estimated vaccine effectiveness (VE) against symptomatic infection and severe outcomes (hospitalization or death) caused by Omicron or Delta between December 6 and 26, 2021. We used multivariable logistic regression to estimate the effectiveness of 2 or 3 COVID-19 vaccine doses by time since the latest dose, compared to unvaccinated individuals. Results We included 16,087 Omicron-positive cases, 4,261 Delta-positive cases, and 114,087 test-negative controls. VE against symptomatic Delta infection declined from 89% (95%CI, 86-92%) 7-99 days after a second dose to 80% (95%CI, 74-84%) after >=240 days, but increased to 97% (95%CI, 96-98%) >=7 days after a third dose. VE against symptomatic Omicron infection was only 36% (95%CI, 24-45%) 7-
59 days after a second dose and provided no protection after >=180 days, but increased to 61% (95%CI, 56-65%) >=7 days after a third dose. VE against severe outcomes was very high following a third dose for both Delta and Omicron (99% [95%CI, 98-99%] and 95% [95%CI, 87-98%], respectively). Conclusions In contrast to high levels of protection against both symptomatic infection and severe outcomes caused by Delta, our results suggest that 2 doses of COVID-19 vaccines only offer modest and short-term protection against symptomatic Omicron infection. A third dose improves protection against symptomatic infection and provides excellent protection against severe outcomes for both variants.

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17. Callaway E. Why does the Omicron sub-variant spread faster than the original? Nature. 2022;602(7898):556-7. DOI: 10.1038/d41586-022-00471-2

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Dysregulation in neutrophil extracellular trap (NET) formation and degradation may play a role in the pathogenesis and severity of COVID-19; however, its role in the pediatric manifestations of this disease including MIS-C and chilblain-like lesions (CLL), otherwise known as "COVID toes", remains unclear. Studying multinational cohorts, we found that, in CLL, NETs were significantly increased in serum and skin. There was geographic variability in the prevalence of increased NETs in MIS-C, in association with disease severity. MIS-C and CLL serum samples displayed decreased NET degradation ability, in association with C1q and G-actin or anti-NET antibodies, respectively, but not with genetic variants of DNases. In adult COVID-19, persistent elevations in NETs post-disease diagnosis were detected but did not occur in asymptomatic infection. COVID-19-affected adults displayed significant prevalence of impaired NET degradation, in association with anti-DNase1L3, G-actin, and specific disease manifestations, but not with genetic variants of DNases. NETs were detected in many organs of adult patients who died from COVID-19 complications. Infection with the Omicron variant was associated with decreased levels of NETs compared to other SARS-CoV-2 strains. These data support a role for NETs in the pathogenesis and severity of COVID-19 in pediatric and adult patients. Summary: NET formation and degradation are dysregulated in pediatric and symptomatic adult patients with various complications of COVID-19, in association with disease severity. NET degradation impairments are multifactorial and associated with natural inhibitors of DNase 1, G-actin and anti-DNase1L3 and anti-NET antibodies. Infection with the Omicron variant is associated with decreased levels of NETs when compared to other SARS-CoV-2 strains.

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Background: The magnitude of Omicron SARS-CoV-2 variant of concern (VOC) global spread necessitates reinforcement of surveillance implementation. Conventional VOC surveillance based on genotyping of clinical samples is characterized by certain challenges related to available sequencing capacity, population sampling methodologies, and demands in terms of time, labor, and resources. Wastewater-based SARS-CoV-2 VOC surveillance constitutes a valuable supplementary practice, since it does not require extensive sampling, and provides information on the prevalence of the disease in a timely and cost-effective manner. Method(s): A highly sensitive real-time RT-PCR assay was developed, for targeted Omicron VOC
The ongoing coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has triggered a devastating global health, social and economic crisis. The RNA nature and broad circulation of this virus facilitate the accumulation of mutations, leading to the continuous emergence of variants of concern with increased transmissibility or pathogenicity (1). This poses a major challenge to the effectiveness of current vaccines and therapeutic antibodies (1, 2). Thus, there is an urgent need for effective therapeutic and preventive measures with a broad spectrum of action, especially against variants with an unparalleled number of mutations such as the recently emerged Omicron variant, which is rapidly spreading across the globe (3). Here, we used combinatorial antibody phage-display libraries from convalescent COVID-19 patients to generate monoclonal antibodies against the receptor-binding domain of the SARS-CoV-2 spike protein with ultrapotent neutralizing activity. One such antibody, NE12, neutralizes an early isolate, the WA-1 strain, as well as the Alpha and Delta variants with half-maximal inhibitory concentrations at picomolar level. A second antibody, NA8, has an unusual breadth of neutralization, with picomolar activity against both the Beta and Omicron variants. The prophylactic and therapeutic efficacy of NE12 and NA8 was confirmed in preclinical studies in the golden Syrian hamster model. Analysis by cryo-EM illustrated the structural basis for the neutralization properties of NE12 and NA8. Potent and broadly neutralizing antibodies against conserved regions of the SARS-CoV-2 spike protein may play a key role against future variants of concern that evade immune control.
Evidence Search Report: EOC211220v011 ESR 22

restaurant R1 (19th February 2021), which occurred prior to the mandatory enhancement of indoor air dilution, the secondary attack rate among customers in R2 was significantly lower than that in R1 (3.4%, 7/207 vs 28.9%, 22/76, p<0.001). Enhancement of indoor air dilution through ventilation and installation of air purifier could minimize the risk of SARS-CoV-2 transmission in the restaurants. Copyright © 2022 Elsevier B.V.

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Although vaccines and monoclonal antibody countermeasures have reduced the morbidity and mortality associated with SARS-CoV-2 infection, variants with constellations of mutations in the spike gene threaten their efficacy. Accordingly, antiviral interventions that are resistant to further virus evolution are needed. The host-derived cytokine IFN-lambda has been proposed as a possible treatment based on correlative studies in human COVID-19 patients. Here, we show IFN-lambda protects against SARS-CoV-2 B.1.351 (Beta) and B.1.1.529 (Omicron) variants in three strains of conventional and human ACE2 transgenic mice. Prophylaxis or therapy with nasally-delivered IFN-lambda limited infection of historical or variant (B.1.351 and B.1.1.529) SARS-CoV-2 strains in the upper and lower respiratory tracts without causing excessive inflammation. In the lung, IFN-lambda was produced preferentially in epithelial cells and acted on radio-resistant cells to protect against SARS-CoV-2 infection. Thus, inhaled IFN-lambda may have promise as a treatment for evolving SARS-CoV-2 variants that develop resistance to antibody-based countermeasures.

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Genetic variants of SARS-CoV-2 continue to dramatically alter the landscape of the COVID-19 pandemic. The recently described variant of concern designated Omicron (B.1.1.529) has rapidly spread worldwide and is now responsible for the majority of COVID-19 cases in many countries. Because Omicron was recognized very recently, many knowledge gaps exist about its epidemiology, clinical severity, and disease course. A genome sequencing study of SARS-CoV-2 in the Houston Methodist healthcare system identified 4,468 symptomatic patients with infections caused by Omicron from late November 2021 through January 5, 2022. Omicron very rapidly increased in only three weeks to cause 90% of all new COVID-19 cases, and at the end of the study period caused 98% of new cases. Compared to patients infected with either Alpha or Delta variants in our healthcare system, Omicron patients were significantly younger, had significantly increased vaccine breakthrough rates, and were significantly less likely to be hospitalized. Omicron patients required less intense respiratory support and had a shorter length of hospital stay, consistent with on average decreased disease severity. Two patients with Omicron “stealth”'s sublineage BA.2 also were identified. The data document the unusually rapid spread and increased occurrence of COVID-19 caused by the Omicron variant in metropolitan Houston, and address the lack of information about disease character among US patients. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

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Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread worldwide. Many variants of SARS-CoV-2 have been reported, some of which have increased transmissibility and/or reduced susceptibility to vaccines. There is an urgent need for variant phenotyping for epidemiological surveillance of circulating lineages. Whole-genome sequencing is the gold standard for identifying SARS-CoV-2 variants, which constitutes a major bottleneck in developing countries. Methodological simplification could increase epidemiological surveillance feasibility and efficiency. We designed a novel multiplex real-time reverse transcriptase PCR (RT-PCR) to detect SARS-CoV-2 variants with 5 gene mutations. This multiplex PCR typing method was established to detect 9 mutations with specific primers and probes (DeltaHV 69/70, K417T, K417N, L452R, E484K, E484Q, N501Y, P681H, and P681R) against the receptor-binding domain of the spike protein of SARS-CoV-2 variants. In silico analyses showed high specificity of the assays. Variants of concern (VOC) typing results were found to be highly specific for our intended targets, with no cross-reactivity observed with other upper respiratory viruses. The PCR-based typing methods were further validated using whole-genome sequencing and a commercial kit that was applied to clinical samples of 250 COVID-19 patients from Taiwan. The screening of these samples allowed the identification of epidemic trends by time intervals, including B.1.617.2 in the third Taiwan wave outbreak. This PCR typing strategy allowed the detection of five major variants of concern and also provided an open-source PCR assay which could rapidly be deployed in laboratories around the world to enhance surveillance for the local emergence and spread of B.1.1.7, B.1.351, P.1, and B.1.617.2 variants and of four Omicron mutations on the spike protein (DeltaHV 69/70, K417N, N501Y, P681H).

**IMPORTANCE COVID-19 has spread globally. SARS-CoV-2 variants of concern (VOCs) are leading the next waves of the COVID-19 pandemic. Previous studies have pointed out that these VOCs may have increased infectivity, have reduced vaccine susceptibility, change treatment regimens, and increase the difficulty of epidemic prevention policy. Understanding SARS-CoV-2 variants remains an issue of concern for all local government authorities and is critical for establishing and implementing effective public health measures. A novel SARS-CoV-2 variant identification method based on a multiplex real-time RT-PCR was developed in this study. Five SARS-CoV-2 variants (Alpha, Beta, Gamma, Delta, and Omicron) were identified simultaneously using this method. PCR typing can provide rapid testing results with lower cost and higher feasibility, which is well within the capacity for any diagnostic laboratory. Characterizing these variants and their mutations is important for tracking SARS-CoV-2 evolution and is conducive to public infection control and policy formulation strategies.**

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The SARS-CoV-2 21K/BA.1, 21L/BA.2, and BA.3 Omicron variants have recently emerged worldwide. To date, the 21L/BA.2 Omicron variant has remained very minor globally but became predominant in Denmark instead of the 21K/BA.1 variant. Here we describe the first cases diagnosed with this variant in southeastern France. We identified thirteen cases using variant-specific qPCR and next-generation sequencing between 28/11/2021 and 31/01/2022, the first two cases being diagnosed in travellers returning from Tanzania. Overall, viral genomes displayed a mean (+/- standard deviation) number of 65.9 +/- 2.5 (range, 61-69) nucleotide substitutions and 31.0 +/- 8.3 (27-50) nucleotide deletions, resulting in 49.6 +/- 2.2 (45-52) amino acid substitutions (including 28 in the spike protein) and 12.4 +/- 1.1 (12-15) amino acid deletions. Phylogeny showed the distribution in three different clusters of these genomes, which were most closely related to genomes from England and South Africa, from Singapore and Nepal, or from France and Denmark. Structural predictions highlighted a significant enlargement and flattening of the
surface of the 21L/BA.2 N-terminal domain compared to that of the 21K/BA.1 Omicron variant, which may facilitate initial viral interactions with lipid rafts. Close surveillance is needed at global, country and center scales to monitor the incidence and clinical outcome of the 21L/BA.2 Omicron variant. This article is protected by copyright. All rights reserved.

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On November 26, 2021, the World Health Organization classified B.1.1.529 as a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant of concern (VoC), named omicron. Spike-gene dropouts in conventional SARS-CoV-2 PCR systems have been reported over the last weeks as indirect diagnostic evidence for the identification of omicron. Here, we report the combination of PCRs specific for heavily mutated sites in the spike gene and nanopore-based full-length genome sequencing for the rapid and sensitive identification of the first four COVID-19 patients diagnosed in Germany to be infected with omicron on November 28, 2021. This study will assist the unambiguous laboratory-based diagnosis and global surveillance for this highly contagious VoC with an unprecedented degree of humoral immune escape. Moreover, we propose that specialized diagnostic laboratories should continuously update their assays for variant-specific PCRs in the spike gene of SARS-CoV-2 to readily detect and diagnose emerging variants of interest and VoCs. The combination with established nanopore sequencing procedures allows both the rapid confirmation by whole genome sequencing as well as the sensitive identification of newly emerging variants of this pandemic beta-coronavirus in years to come.

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DOI: 10.1002/jmv.27503


OBJECTIVES: We aimed to compare COVID-19 outcomes in the Omicron-driven fourth wave with prior waves in the Western Cape, the contribution of undiagnosed prior infection to differences in outcomes in a context of high seroprevalence due to prior infection, and whether protection against severe disease conferred by prior infection and/or vaccination was maintained. METHODS: In this cohort study, we included public sector patients aged >/=20 years with laboratory confirmed COVID-19 diagnosis between 14 November-11 December 2021 (wave four) and equivalent prior wave periods. We compared the risk between waves of the following outcomes using Cox regression: death, severe hospitalization or death and any hospitalization or death (all </=14 days after diagnosis) adjusted for age, sex, comorbidities, geography, vaccination and prior infection. RESULTS: We included 5,144 patients from wave four and 11,609 from prior waves. Risk of all outcomes was lower in wave four compared to the Delta-driven wave three (adjusted Hazard Ratio (aHR) [95% confidence interval (CI)] for death 0.27 [0.19; 0.38]. Risk reduction was lower when adjusting for vaccination and prior diagnosed infection (aHR:0.41, 95% CI: 0.29; 0.59) and reduced further when accounting for unascertained prior infections (aHR:0.72). Vaccine protection was maintained in wave four (aHR for outcome of death: 0.24; 95% CI: 0.10; 0.58). CONCLUSIONS: In the Omicron-driven wave, severe COVID-19 outcomes were reduced mostly due to protection conferred by
prior infection and/or vaccination, but intrinsically reduced virulence may account for an approximately 25% reduced risk of severe hospitalization or death compared to Delta.

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Importance: Outpatient physicians need guidance to support their clinical decisions regarding management of patients with COVID-19, specifically whether to hospitalize a patient or if managed as an outpatient, how closely to follow them. Objective(s): To develop and prospectively validate a clinical prediction rule to predict the likelihood of hospitalization for outpatients with COVID-19 that does not require laboratory testing or imaging, including during the current Omicron wave. Design(s): Derivation and temporal validation of a clinical prediction rule, and prospective validation of two externally derived clinical prediction rules. Setting(s): Primary and urgent care clinics in a Pennsylvania health system. Participant(s): Patients 12 years and older presenting to outpatient clinics who had a positive polymerase chain reaction test for COVID-19. Main Outcomes and Measures: Classification accuracy (percentage in each risk group hospitalized) and area under the receiver operating characteristic curve (AUC). Result(s): Overall, 4.0% of outpatients in the early derivation cohort (5843 patients presenting before 3/1/21), 4.2% in the late validation cohort (3806 patients presenting 3/1/21 to 9/30/21), and 1.9% in an Omicron cohort were ultimately hospitalized. We developed and temporally validated four simple risk scores. The base score included age, dyspnea, and the presence of a comorbidity, with the other scores adding fever, respiratory rate and/or oxygen saturation. All had very good overall accuracy (AUC 0.85-0.87) and classified at least half of patients into a low risk with a < 1% likelihood of hospitalization. Hospitalization rates in the Omicron cohort were 0.22%, 1.3% and 8.7% for the base score. Two externally derived risk scores identified more low risk patients, but with a higher overall risk of hospitalization than our novel risk scores. Conclusions and relevance: A simple risk score applicable to outpatient and telehealth settings can classify over half of COVID-19 outpatients into a very low risk group with a 0.22% hospitalization risk in the Omicron cohort. The Lehigh Outpatient COVID Hospitalization (LOCH) risk score is available online as a free app: https://ebell-projects.shinyapps.io/LehighRiskScore/. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

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The impact of vaccination and new SARS-CoV-2 variants on peri-operative outcomes is unclear. We aimed to update previously published consensus recommendations on timing of elective surgery after SARS-CoV-2 infection to assist policymakers, administrative staff, clinicians and patients. The guidance remains that patients should avoid elective surgery within 7 weeks of infection, unless the benefits of doing so exceed the risk of waiting. We recommend individualised multidisciplinary risk assessment for patients requiring elective surgery within 7 weeks of SARS-CoV-2 infection. This should include baseline mortality risk
calculation and assessment of risk modifiers (patient factors; SARS-CoV-2 infection; surgical factors). Asymptomatic SARS-CoV-2 infection with previous variants increased peri-operative mortality risk three-fold throughout the 6 weeks after infection, and assumptions that asymptomatic or mildly symptomatic omicron SARS-CoV-2 infection does not add risk are currently unfounded. Patients with persistent symptoms and those with moderate-to-severe COVID-19 may require a longer delay than 7 weeks. Elective surgery should not take place within 10 days of diagnosis of SARS-CoV-2 infection, predominantly because the patient may be infectious, which is a risk to surgical pathways, staff and other patients. We now emphasise that timing of surgery should include the assessment of baseline and increased risk, optimising vaccination and functional status, and shared decision-making. While these recommendations focus on the omicron variant and current evidence, the principles may also be of relevance to future variants. As further data emerge, these recommendations may be revised.

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The unprecedented rise in SARS-CoV-2 infections during December 2021 was concurrent with rapid spread of the Omicron variant in England and globally. We analyzed prevalence of SARS-CoV-2 and its dynamics in England from end November to mid-December 2021 among almost 100,000 participants from the REACT-1 study. Prevalence was high with rapid growth nationally and particularly in London during December 2021, and an increasing proportion of infections due to Omicron. We observed large falls in swab positivity among mostly vaccinated older children (12-17 years) compared with unvaccinated younger children (5-11 years), and in adults who received a third (booster) vaccine dose vs. two doses. Our results reinforce the importance of vaccination and booster campaigns, although additional measures have been needed to control the rapid growth of the Omicron variant.

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SARS-CoV-2 lineages have diverged into highly prevalent variants termed "variants of concern" (VOCs). Here, we characterized emerging SARS-CoV-2 spike polymorphisms in vitro and in vivo to understand their impact on transmissibility and virus pathogenicity and fitness. We demonstrate that the substitution S:655Y, represented in the gamma and omicron VOCs, enhances viral replication and spike protein cleavage. The S:655Y substitution was transmitted more efficiently than its ancestor S:655H in the hamster infection model and was able to outcompete S:655H in the hamster model and in a human primary airway system. Finally, we analyzed a set of emerging SARS-CoV-2 variants to investigate how different sets of mutations may impact spike processing. All VOCs tested exhibited increased spike cleavage and fusogenic capacity. Taken together, our study demonstrates that the spike mutations present in VOCs that become epidemiologically prevalent in humans are linked to an increase in spike processing and virus transmission.

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The Omicron variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has high transmissibility and recently swept the globe. Due to the extensive number of mutations, this variant has high level of immune evasion, which drastically reduced the efficacy of existing antibodies and vaccines. Thus, it is
important to test an Omicron-specific vaccine, evaluate its immune response against Omicron and other variants, and compare its immunogenicity as boosters with existing vaccine designed against the reference wildtype virus (WT). Here, we generated an Omicron-specific lipid nanoparticle (LNP) mRNA vaccine candidate, and tested its activity in animals, both alone and as a heterologous booster to existing WT mRNA vaccine. Our Omicron-specific LNP-mRNA vaccine elicited strong and specific antibody response in vaccination-naive mice. Mice that received two-dose WT LNP-mRNA, the one mimicking the commonly used Pfizer/Moderna mRNA vaccine, showed a >40-fold reduction in neutralization potency against Omicron variant than that against WT two weeks post second dose, which further reduced to background level >3 months post second dose. As a booster shot for two-dose WT mRNA vaccinated mice, a single dose of either a homologous booster with WT LNP-mRNA or a heterologous booster with Omicron LNP-mRNA restored the waning antibody response against Omicron, with over 40-fold increase at two weeks post injection as compared to right before booster. Interestingly, the heterologous Omicron LNP-mRNA booster elicited neutralizing titers 10-20 fold higher than the homologous WT booster against the Omicron variant, with comparable titers against the Delta variant. All three types of vaccination, including Omicron mRNA alone, WT mRNA homologous booster, and Omicron heterologous booster, elicited broad binding antibody responses against SARS-CoV-2 WA-1, Beta, and Delta variants, as well as other Betacoronavirus species such as SARS-CoV, but not Middle East respiratory syndrome coronavirus (MERS-CoV). These data provided direct proof-of-concept assessments of an Omicron-specific mRNA vaccination in vivo, both alone and as a heterologous booster to the existing widely-used WT mRNA vaccine form.

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Variants of SARS-CoV-2 may evade natural and vaccine induced immunity and monoclonal antibody immunotherapeutics. There is an urgent need to know how well antibodies, induced by healthy and Clinically Extremely Vulnerable (CEV) patients, will bind and thus help reduce transmission and severity of infection from variants of concern (VOC). This study determines the cross-reactive binding of serum antibodies obtained prior to and 28 days after a third vaccination in three cohorts: a health care worker cohort who received three doses of Pfizer-BioNTech (PPP), a cohort of CEV patients received two doses of the AstraZeneca-ChAdOx1-nCoV-19 (AAP) vaccine, followed by a third PFZ vaccine and a haemodialysis cohort that had a mixture of two AZ or PFZ vaccines followed by a PFZ booster. Six months post second vaccine there was evidence of antibody waning with 58.9% of individuals in the HD cohort seropositive against Wuhan, 34.4% Delta and 62.2% Omicron strains. For the AAP cohort, equivalent figures were 62.5%, 45.8% and 91.7% and the PPP cohort 92.2%, 90% and 91.1%. Post third dose vaccination there were universal increases in seropositivity and median optical density. For the HD cohort, 98.8% were seropositive to the Wuhan strain, 97.6% against Delta and 100% against Omicron strains. For the PPP and AAP cohorts, 100% were seropositive against all 3 strains. Lastly, we examined the WHO NIBSC 20/136 standard and there was no loss of antibody binding to either VOC. Similarly, a dilution series of Sotrovimab (GSK) found this therapeutic monoclonal antibody bound similarly to all VOC. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-ND 4.0 International license.

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BACKGROUND: Five SARS-CoV-2 variants are currently considered as variants of concern (VOC). Omicron was declared a VOC at the end of November 2021. Based on different diagnostic methods, the occurrence of Omicron was reported by 52 countries worldwide on December 7 2021. First notified by South Africa with alarming reports on increasing infection rates, this new variant was soon suspected to replace the
currently pre-dominating Delta variant leading to further infection waves worldwide. METHODS: Using VOC PCR screening and Next Generation Sequencing (NGS) analysis of selected samples, we investigated the circulation of Omicron in the German federal state Bavaria. For this, we analyzed SARS-CoV-2 surveillance data from our laboratory generated from calendar week (CW) 01 to 49/2021. RESULTS: So far, we have detected 69 Omicron cases in our laboratory from CW 47-49/2021 using RT-qPCR followed by melting curve analysis. The first 16 cases were analyzed by NGS and all were confirmed as Omicron. CONCLUSION: Our data strongly support no circulation of the new Omicron variant before CW 47/2021.

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Convalescent plasma (CP) recurs as a frontline treatment in epidemics because it is available as soon as there are survivors. The COVID-19 pandemic represented the first large-scale opportunity to shed light on the mechanisms of action, safety, and efficacy of CP using modern evidence-based medicine approaches. Studies ranging from observational case series to randomized controlled trials (RCTs) have reported highly variable efficacy results for COVID-19 CP (CCP), resulting in uncertainty. We analyzed variables associated with efficacy, such as clinical settings, disease severity, CCP SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) antibody levels and function, dose, timing of administration (variously defined as time from onset of symptoms, molecular diagnosis, diagnosis of pneumonia, or hospitalization, or by serostatus), outcomes (defined as hospitalization, requirement for ventilation, clinical improvement, or mortality), CCP provenance and time for collection, and criteria for efficacy. The conflicting trial results, along with both recent WHO guidelines discouraging CCP usage and the recent expansion of the FDA emergency use authorization (EUA) to include outpatient use of CCP, create confusion for both clinicians and patients about the appropriate use of CCP. A review of 30 available RCTs demonstrated that signals of efficacy (including reductions in mortality) were more likely if the CCP neutralizing titer was >160 and the time to randomization was less than 9 days. The emergence of the Omicron variant also reminds us of the benefits of polyclonal antibody therapies, especially as a bridge to the development and availability of more specific therapies.

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COVID-19 emergency use authorizations and approvals for vaccines were achieved in record time. However, there remains a need to develop additional safe, effective, easy-to-produce, and inexpensive prevention to reduce the risk of acquiring SARS-CoV-2 infection. This need is due to difficulties in vaccine manufacturing and distribution, vaccine hesitancy, and, critically, the increased prevalence of SARS-CoV-2 variants with greater contagiousness or reduced sensitivity to immunity. Antibodies from eggs of hens (immunoglobulin Y; IgY) that were administered receptor-binding domain (RBD) of the SARS-CoV-2 spike protein were developed as nasal drops to capture the virus on the nasal mucosa. Although initially raised against the 2019 novel coronavirus index strain (2019-nCoV), these anti-SARS-CoV-2 RBD IgY surprisingly had indistinguishable enzyme-linked immunosorbent assay binding against variants of concern that have emerged, including Alpha (B.1.1.7), Beta (B.1.351), Delta (B.1.617.2), and Omicron (B.1.1.529). This is distinct for sera from immunized or convalescent patients. Culture neutralization titers against available Alpha, Beta, and Delta were also indistinguishable from the index SARS-CoV-2 strain. Efforts to develop these IgY for clinical use demonstrated that the intranasal anti-SARS-CoV-2 RBD IgY preparation showed no binding (cross-reactivity) to a variety of human tissues and had an excellent safety profile in rats following 28-day intranasal delivery of the formulated IgY. A double-blind, randomized, placebo-controlled phase 1 study evaluating single-ascending and multiple doses of anti-SARS-CoV-2 RBD IgY
administered intranasally for 14 days in 48 healthy participants also demonstrated an excellent safety and tolerability profile, and no evidence of systemic absorption. As these antiviral IgY have broad selectivity against many variants of concern, are fast to produce, and are a low-cost product, their use as prophylaxis to reduce SARS-CoV-2 viral transmission warrants further evaluation. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC-ND 4.0 International license.

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Emerging SARS-CoV-2 variants of concern (VOC) have been associated with enhanced transmissibility and immune escape. Next-generation sequencing (NGS) of the whole genome is the gold standard for variant identification for surveillance but is time-consuming and costly. Rapid and cost-effective assays that detect SARS-CoV-2 variants are needed. We evaluated Allplex SARS-CoV-2 Master Assay and Variants I Assay to detect HV69/70 deletion, Y144 deletion, E484K, N501Y, and P681H spike mutations in 248 positive samples collected in Kuala Lumpur, Malaysia, between January and May 2021. Spike variants were detected in 78/248 (31.5%), comprising 60 VOC B.1.351 (beta) and 18 B.1.1.7 (alpha). With NGS as reference for 115 samples, the sensitivity for detecting the spike mutations was 98.7% with the Master Assay and 100% with the Variants I Assay. The emergence of beta variants correlated with increasing COVID-19 infections in Malaysia. The prevalence of alpha VOC and lineage B.1.466.2 was low. These assays detect mutations present in alpha, beta and gamma VOCs. Of the VOCs which have subsequently emerged, the assays should detect omicron (B.1.1.529) but not B.1.617.2 (delta). In conclusion, spike variant PCR assays can be used to rapidly monitor selected SARS-CoV-2 VOCs in resource-limited settings, but require updates as new variants emerge.

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DOI: 10.1016/j.jviromet.2022.114462


To investigate the induction of neutralizing antibodies against Omicron after two and three vaccine doses in recipients of different ages. Physicians at Kobe University Hospital who had received the second dose of the BNT162b2 mRNA vaccine. At 2 months after the second vaccinations, the positive rate of neutralizing antibody against Omicron was 28%, and the titer was significantly lower than those against other variants, 11.8-fold and 3.6-fold lower than those against D614G and Delta, respectively. Unlike Delta, that positive rates of neutralizing antibody against Omicron were low in all age groups, and there was no significant difference in titers among age groups. Seven months after the 2nd dose, the positive rate of neutralizing antibody against Omicron decreased to 6%, but after the booster, 3rd vaccination, it increased to 100%, and the titer was much higher than those at 2 and 7 months post-vaccination, 32-fold and 39-fold respectively. The booster vaccination effect was also observed in the younger at 41-fold, middle-aged at 43-fold, and older at 27-fold groups compared to the 7-month titers. Surprisingly, higher-than-predicted titers of the neutralizing antibodies against Omicron were induced after the booster vaccination regardless of recipient age, while this effect was not observed after two doses, indicating the induction of antibodies against common epitopes by the booster vaccination. Three doses can be confidently recommended to suppress the pandemic. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

DOI: 10.1101/2022.01.25.22269735
Background: Since identification, infections by new SARS-CoV-2 variant Omicron are rapidly increasing worldwide. There is huge gap of knowledge regarding virus behaviour in the population from low and middle income countries. Delhi being unique population with a high seropositivity and vaccination rate against COVID-19 infection. We aimed to study the epidemiological and clinical presentations of few early cases of community spread of Omicron infection in the state. Method(s): This is a prospective study where respiratory specimen from all RT-PCR confirmed positive cases between November 25th-December 23rd 2021 collected from five districts of Delhi were subjected to whole genome sequencing. Complete demographic and clinical details were recorded. We also analyzed the formation of local and familial clusters and eventual community transmission. Finding(s): Out of the 264 cases included during study period, 68.9% (n=182) were identified as Delta and its sub-lineages while 31.06% (n=82) were Omicron with BA.1 as the predominant sub-lineage (73.1%). Most of the Omicron cases were asymptomatic (n=50, 61%) and not requiring any hospitalizations. A total of 72 (87.8%) cases were fully vaccinated. 39.1% (n=32) had a history of travel and/or contacts while 60.9 (n=50) showed a community transmission. A steep increase in the daily progression of Omicron cases with its preponderance in the community was observed from 1.8% to 54%. Interpretation(s): This study is among the first from India to provide the evidence of community transmission of Omicron with significantly increased breakthrough infections, decreased hospitalization rates, and lower rate of symptomatic infections among individuals with high seropositivity against SARS-CoV-2 infections.


Since the inception of SARS-CoV-2 in December 2019, many variants have emerged over time. Some of these variants have resulted in transmissibility changes of the virus and may also have impact on diagnosis, therapeutics and even vaccines, thereby raising particular concerns in the scientific community. The variants which have mutations in Spike glycoprotein are the primary focus as it is the main target for neutralising antibodies. SARS-CoV-2 is known to infect human through Spike glycoprotein and uses receptor-binding domain (RBD) to bind to the ACE2 receptor in human. Thus, it is of utmost importance to study these variants and their corresponding mutations. Such 12 different important variants identified so far are B.1.1.7 (Alpha), B.1.351 (Beta), B.1.427/B.1.429 (Epsilon), B.1.526 (Iota), B.1.617.1 (Kappa), B.1.617.2 (Delta), C.37 (Lambda), P.1 (Gamma), P.2 (Zeta), P.3 (Theta) and the recently discovered B.1.1.529 (Omicron). These variants have 84 unique mutations in Spike glycoprotein. To analyse such mutations, multiple sequence alignment of 77681 SARS-CoV-2 genomes of 98 countries over the period from January 2020 to July 2021 is performed followed by phylogenetic analysis. Also, characteristics of new emerging variants are elaborately discussed. The individual evolution of these mutation points and the respective variants are visualised and their characteristics are also reported. Moreover, to judge the characteristics of the non-synonymous mutation points (substitutions), their biological functions are evaluated by PolyPhen-2 while protein structural stability is evaluated using I-Mutant 2.0.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35123183
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The SARS-CoV-2 Omicron strain emergence raised concerns that its enhanced infectivity is partly due to altered spread/contamination modalities. We therefore sampled high-contact surfaces and air in close proximity to patients verified as infected with Omicron strain, using identical protocols applied to sample patients positive to the original or Alpha strains. Cumulatively, for all three strains, viral RNA was detected in 90/168 surfaces and 6/49 air samples (mean Ct=35.2+/−2.5). No infective virus was identified. No significant differences in prevalence were found between strains.

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DOI: 10.1016/j.ijid.2022.03.001


Our study focuses on free energy calculations of SARS-CoV-2 spike protein receptor binding motives (RBMs) from wild type and variants of concern (VOCs), with emphasis on SARS-CoV-2 Omicron. Our computational analysis underlines the occurrence of positive selection processes that specify Omicron host adaption and bring changes on the molecular level into context with clinically relevant observations. Our free energy calculation studies regarding the interaction of Omicron’s RBM with human angiotensin converting enzyme 2 (hACE2) indicate weaker binding to the receptor than Alpha’s or Delta’s RBMs. Upon weaker binding, fewer viruses are predicted to be generated in time per infected cell, resulting in a delayed induction of danger signals as a trade-off. Along with delayed immunogenicity and pathogenicity, more viruses may be produced in the upper respiratory tract, explaining enhanced transmissibility. Since in interdependence on the human leukocyte antigen type (HLA type), more SARS-CoV-2 Omicron viruses are assumed to be required to initiate inflammatory immune responses, and because of pre-existing partial immunity through previous infections and/or vaccinations, which mostly guard the lower respiratory tract, overall disease severity is expected to be reduced.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35208550
DOI: 10.3390/medicina58020226

Aided by extensive spike protein mutation, the SARS-CoV-2 Omicron variant overtook the previously dominant Delta variant. Spike conformation plays an essential role in SARS-CoV-2 evolution via changes in receptor binding domain (RBD) and neutralizing antibody epitope presentation affecting virus transmissibility and immune evasion. Here, we determine cryo-EM structures of the Omicron and Delta spikes to understand the conformational impacts of mutations in each. The Omicron spike structure revealed an unusually tightly packed RBD organization with long range impacts that were not observed in the Delta spike. Binding and crystallography revealed increased flexibility at the functionally critical fusion peptide site in the Omicron spike. These results reveal a highly evolved Omicron spike architecture with possible impacts on its high levels of immune evasion and transmissibility.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35118469
DOI: 10.1101/2022.01.25.477784


After the implementation of broad vaccination programs, there is an urgent need to understand how the population immunity affects the dynamics of the COVID-19 pandemic in presence of the protection waning and of the emergence of new variants of concern. In the current Omicron wave that is propagating across Europe, assessing the risk of saturation of the healthcare systems is crucial for pandemic management, as it allows us to support the transition towards the endemic course of SARS-CoV-2 and implement more refined mitigation strategies that shield the most vulnerable groups and protect the healthcare systems. We investigated the current pandemic dynamics by means of compartmental models that describe the age-stratified social-mixing, and consider vaccination status, vaccine types, and their waning efficacy. Our goal is to provide insight into the plausible scenarios that are likely to be seen in Switzerland and Germany in the coming weeks and help take informed decisions. Despite the huge numbers of new positive cases, our results suggest that the current wave is unlikely to create an overwhelming healthcare demand: owing to the lower hospitalization rate of the novel variant and the effectiveness of the vaccines. Our findings are robust with respect to the plausible variability of the main parameters that govern the severity and the progression of the Omicron infection. In a broader context, our framework can be applied also to future endemic scenarios, offering quantitative support for refined public health interventions in response to recurring COVID-19 waves. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC-ND 4.0 International license.

DOI: 10.1101/2022.01.24.22269676


We develop a stochastic, multi-strain, compartmental epidemic model to estimate the relative transmissibility and immune escape of the Omicron variant of concern (VOC) in South Africa. The model integrates population, non-pharmaceutical interventions, vaccines, and epidemiological data and it is calibrated in the period May 1st, 2021 - November 23rd, 2021. We explore a parameter space of relative transmissibility with respect to the Delta variant and immune escape for Omicron by assuming an initial seeding, from unknown origin, in the first week of October 2021. We identify a region of the parameter space where combinations of relative transmissibility and immune escape are compatible with the growth of the epidemic wave. We also find that changes in the generation time associated with Omicron infections strongly affect the results concerning its relative transmissibility. The presented results are informed by current knowledge of Omicron and subject to changes. Copyright The copyright holder for this
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Omicron, the novel highly mutated SARS-CoV-2 Variant of Concern (VOC, Pango lineage B.1.1.529) was first collected in early November 2021 in South Africa. By the end of November 2021, it had spread and approached fixation in South Africa, and had been detected on all continents. We analyzed the exponential growth of Omicron over four-week periods in the two most populated of South Africa's provinces, Gauteng and KwaZulu-Natal, arriving at the doubling time estimates of, respectively, 3.3 days (95% CI: 3.2-3.4 days) and 2.7 days (95% CI: 2.3-3.3 days). Similar or even shorter doubling times were observed in other locations: Australia (3.0 days), New York State (2.5 days), UK (2.4 days), and Denmark (2.0 days). Log-linear regression suggests that the spread began in Gauteng around 11 October 2021; however, due to presumable stochasticity in the initial spread, this estimate can be inaccurate.

Phylogenetics-based analysis indicates that the Omicron strain started to diverge between 6 October and 29 October 2021. We estimated that the weekly growth of the ratio of Omicron to Delta is in the range of 7.2-10.2, considerably higher than the growth of the ratio of Delta to Alpha (estimated to be in the range of 2.5-4.2), and Alpha to pre-existing strains (estimated to be in the range of 1.8-2.7). High relative growth does not necessarily imply higher Omicron infectivity. A two-strain SEIR model suggests that the growth advantage of Omicron may stem from immune evasion, which permits this VOC to infect both recovered and fully vaccinated individuals. As we demonstrated within the model, immune evasion is more concerning than increased transmissibility, because it can facilitate larger epidemic outbreaks.

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SARS-CoV-2 variants of concern (VOCs) continue to pose a public health threat which necessitates a real-time monitoring strategy to compliment whole genome sequencing. Thus, we investigated the efficacy of competitive probe RT-qPCR assays for six mutation sites identified in SARS-CoV-2 VOCs and, after validating the assays with synthetic RNA, performed these assays on positive saliva samples. When compared with whole genome sequence results, the SDelta69-70 and ORF1aDelta3675-3677 assays demonstrated 93.60% and 68.00% accuracy, respectively. The SNP assays (K417T, E484K, E484Q, L452R) demonstrated 99.20%, 96.40%, 99.60%, and 96.80% accuracies, respectively. Lastly, we screened 345 positive saliva samples from December 7-22, 2021 using Omicron-specific mutation assays and were able to quickly identify rapid spread of Omicron in Upstate South Carolina. Our workflow demonstrates a novel approach for low-cost, real-time population screening of VOCs. Importance: SARS-CoV-2 variants of concern and their many sublineages can be characterized by mutations present within their genetic sequences. These mutations can provide selective advantages such as increased transmissibility and antibody evasion, which influences public health recommendations such as mask mandates, quarantine requirements, and treatment regimens. Our real-time RT-qPCR workflow allows for strain identification of SARS-CoV-2 positive saliva samples by targeting common mutation sites shared between VOCs and detecting single nucleotides present at the targeted location. This differential diagnostic system can quickly and effectively identify a wide array of SARS-CoV-2 strains, which can provide more informed public health surveillance strategies in the future.

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DOI: 10.1101/2022.03.02.22271785
Evidence Search Report: EOC211220v011 ESR


The coronavirus disease 2019 (COVID-19) pandemic continues worldwide with many variants arising, some of which are variants of concern (VOCs). A recent VOC, omicron (B.1.1.529), which obtains a large number of mutations in the receptor-binding domain (RBD) of the spike protein, has risen to intense scientific and public attention. Here, we studied the binding properties between the human receptor ACE2 (hACE2) and the VOC RBDs and resolved the crystal and cryo-electron microscopy structures of the omicron RBD-hACE2 complex as well as the crystal structure of the delta RBD-hACE2 complex. We found that, unlike alpha, beta, and gamma, omicron RBD binds to hACE2 at a similar affinity to that of the prototype RBD, which might be due to compensation of multiple mutations for both immune escape and transmissibility. The complex structures of omicron RBD-hACE2 and delta RBD-hACE2 reveal the structural basis of how RBD-specific mutations bind to hACE2.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35093192
DOI: 10.1016/j.cell.2022.01.001


The emergence and rapid global spread of the new Delta and, more recently, Omicron variants of SARS-CoV-2 pose a daunting public health emergency. Being an RNA virus, the Covid-19 virus is continuing to mutate, resulting in the emergence of new variants with high transmissibility, such as the recently discovered Omicron variant. In this paper, we consider the conditions that may facilitate viral mutations and the emergence of variants with the ability to evade immunity. Here, we have discussed the importance of vaccination with the currently available vaccines. These vaccines are highly effective at preventing serious disease, hospitalization, and death from Covid-19. However, the antibody response induced by these vaccines is short-lasting and there are reports of breakthrough infections. A stable and persistent interaction between T follicular helper cells and germinal center B cells is needed for robust B cell memory response. We discussed the potential reasons behind the breakthrough infections and underscored the importance of developing better second-generation vaccines that may not necessitate frequent booster immunizations and are preventive in nature. This may involve the development of multivalent vaccines and creating vaccines against other viral proteins including conserved proteins. Vaccine hesitancy remains a notable hurdle for implementing vaccination. Furthermore, we recommend different approaches to increase vaccine acceptance, which is a critical translational component of a successful vaccine strategy. These perspectives on overcoming the pandemic’s current challenges provide strategies to contain SARS-CoV-2 globally.

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DOI: 10.1016/j.jaut.2021.102792


Scattered reports have suggested that as many as one-half of all hospital inpatients identified as COVID-positive are incidental cases who were admitted primarily for reasons other than their viral infections. To date, however, there are no systematic studies of a representative panel of hospitals based on pre-established criteria for determining whether an individual patient was in fact admitted as a result of the disease. To fill this gap, we developed a formula to estimate the fraction of incidental COVID hospitalizations that relies upon measurable, population-based parameters. We applied this approach to a longitudinal panel of 164 counties throughout the United States, covering a 4-week interval ending in the first week of January 2022. Within this panel, we estimated that COVID incidence has been rising exponentially at a rate of 9.34% per day (95% CI, 8.93-9.87). Assuming that only one-quarter of all recent Omicron infections have been reported by public authorities, we further estimated the aggregate prevalence of active SARS-CoV-2 infection during the first week of January to be 4.89%. During the same week, among 250 high-COVID-volume hospitals within our 164-county panel, an estimated 1 in 4 inpatients was COVID-positive. Among
such COVID-positive hospitalized patients, 15.2% were estimated to be incidental infections. Across individual counties, the median fraction of incidental COVID hospitalizations was 13.7%, with an interquartile range of 9.5 to 18.4%. Incidental COVID infections appear to be a non-trivial fraction of all COVID-positive hospitalized patients. In the aggregate, however, the burden of patients admitted for complications of their viral infections appears to be far greater.

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**BACKGROUND:** In May, 2021, the delta (B.1.617.2) SARS-CoV-2 variant became dominant in the UK, superseded by the omicron (B.1.1.529) variant in December, 2021. The delta variant is associated with increased transmissibility compared with the alpha variant, which was the dominant variant in the UK between December, 2020, and May, 2021. To understand transmission and the effectiveness of interventions, we aimed to investigate whether the delta variant generation time (the interval between infections in infector-infected pairs) is shorter - ie, transmissions are happening more quickly - than that of the alpha variant. **METHODS:** In this epidemiological analysis, we analysed transmission data from an ongoing UK Health Security Agency (UKHSA) prospective household study. Households were recruited to the study after an index case had a positive PCR test and genomic sequencing was used to determine the variant responsible. By fitting a mathematical transmission model to the data, we estimated the intrinsic generation time (which assumes a constant supply of susceptible individuals throughout infection) and the household generation time (which reflects realised transmission in the study households, accounting for susceptible depletion) for the alpha and delta variants. **FINDINGS:** Between February and August, 2021, 227 households consisting of 559 participants were recruited to the UKHSA study. The alpha variant was detected or assumed to be responsible for infections in 131 households (243 infections in 334 participants) recruited in February - May, and the delta variant in 96 households (174 infections in 225 participants) in May - August. The mean intrinsic generation time was shorter for the delta variant (4.7 days, 95% credible interval [CI] 4.1 - 5.6) than the alpha variant (5.5 days, 4.7 - 6.5), with 92% posterior probability. The mean household generation time was 28% (95% CI 0 - 48%) shorter for the delta variant (3.2 days, 95% CI 2.5 - 4.2) than the alpha variant (4.5 days, 3.7 - 5.4), with 97.5% posterior probability. **INTERPRETATION:** The delta variant transmits more quickly in households than the alpha variant, which can be attributed to faster depletion of susceptible individuals in households and a possible decrease in the intrinsic generation time. Interventions such as contact tracing, testing, and isolation might be less effective if transmission of the virus occurs quickly. **FUNDING:** National Institute for Health Research, UK Health Security Agency, Engineering and Physical Sciences Research Council, and UK Research and Innovation.

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DOI: 10.1016/S1473-3099(22)00001-9


Background. The Omicron SARS-CoV-2 variant is responsible for a major wave of COVID-19, with record case counts reflecting high transmissibility and escape from prior immunity. Defining the time course of Omicron viral proliferation and clearance is crucial to inform isolation protocols aiming to minimize disease spread. Methods. We obtained longitudinal, quantitative RT-qPCR test results using combined anterior nares and oropharyngeal samples (n = 10,324) collected between July 5th, 2021 and January 10th, 2022 from the National Basketball Association’s (NBA) occupational health program. We quantified the fraction of tests with PCR cycle threshold (Ct) values <30, chosen as a proxy for potential infectivity and antigen test positivity, on each day after first detection of suspected and confirmed Omicron infections, stratified by individuals detected under frequent testing protocols and those detected due to
symptom onset or concern for contact with an infected individual. We quantified the duration of viral proliferation, clearance rate, and peak viral concentration for individuals with acute Omicron and Delta variant SARS-CoV-2 infections. Results. A total of 97 infections were confirmed or suspected to be from the Omicron variant and 107 from the Delta variant. Of 27 Omicron-infected individuals testing positive <=1 day after a previous negative or inconclusive test, 52.0% (13/25) were PCR positive with Ct values <30 at day 5, 25.0% (6/24) at day 6, and 13.0% (3/23) on day 7 post detection. Of 70 Omicron-infected individuals detected >=2 days after a previous negative or inconclusive test, 39.1% (25/64) were PCR positive with Ct values <30 at day 5, 33.3% (21/63) at day 6, and 22.2% (14/63) on day 7 post detection. Overall, Omicron infections featured a mean duration of 9.87 days (95% CI 8.83-10.9) relative to 10.9 days (95% CI 9.41-12.4) for Delta infections. The peak viral RNA based on Ct values was lower for Omicron infections than for Delta infections (Ct 23.3, 95% CI 22.4-24.3 for Omicron; Ct 20.5, 95% CI 19.2-21.8 for Delta) and the clearance phase was shorter for Omicron infections (5.35 days, 95% CI 4.78-6.00 for Omicron; 6.23 days, 95% CI 5.43-7.17 for Delta), though the rate of clearance was similar (3.13 Ct/day, 95% CI 2.75-3.54 for Omicron; 3.15 Ct/day, 95% CI 2.69-3.64 for Delta). Conclusions. While Omicron infections feature lower peak viral RNA and a shorter clearance phase than Delta infections on average, it is unclear to what extent these differences are attributable to more immunity in this largely vaccinated population or intrinsic characteristics of the Omicron variant. Further, these results suggest that Omicron's infectiousness may not be explained by higher viral load measured in the nose and mouth by RT-PCR. The substantial fraction of individuals with Ct values <30 at days 5 of infection, particularly in those detected due to symptom onset or concern for contact with an infected individual, underscores the heterogeneity of the infectious period, with implications for isolation policies.

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The SARS-CoV-2 Omicron exhibits striking immune evasion and is spreading rapidly worldwide. Understanding the structural basis of the high transmissibility and enhanced immune evasion of Omicron is of high importance. Here through cryo-EM analysis, we present both the closed and open states of the Omicron spike (S), which appear more compact than the counterparts of the G614 strain(1), potentially related to Omicron residue substitutions-induced enhanced inter-protomer and S1-S2 interactions. The closed state showing dominant population may indicate a conformational masking mechanism for Omicron's immune evasion. Moreover, we capture three states for the Omicron S-ACE2 complex, revealing that the substitutions on the Omicron RBM result in new salt bridges/H-bonds, more favorable electrostatic surface properties, and overall strengthened S-ACE2 interaction, in line with the observed higher ACE2 affinity of Omicron S relative to G614. Furthermore, we determine structures of Omicron S in complex with the Fab of S3H3, an antibody able to cross-neutralize major variants of concern including Omicron, elucidating the structural basis for S3H3-mediated broad-spectrum neutralization. Our findings shed new lights on the receptor engagement and antibody neutralization/evasion of Omicron and may also inform design of broadly effective SARS-CoV-2 vaccines.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35228716
DOI: 10.1038/s41586-022-04581-9


PURPOSE OF REVIEW: The current article reviews the latest information on the epidemiology, clinical features, diagnostics, clinical management and prevention of coronavirus disease 2019 (COVID-19). RECENT FINDINGS: Atypical pneumonia due to severe acute respiratory syndrome coronavirus-2 emerged in December 2019 in a market in Wuhan, China and rapidly evolved into a pandemic in March 2020. Viral
loads of patients with COVID-19 peak in the first week of illness around day 2-4 and hence there is very high-transmission potential causing community outbreaks. Asymptomatic and presymptomatic transmission is a hallmark of COVID-19. Several variants of concern (VOC) have emerged over the last 2 years and Omicron is the predominant variant in many countries. PCR is the standard diagnostic test while rapid antigen test is a useful supplementary test. Serology tests provide indirect evidence of infection 1-2 weeks after the onset of symptoms. Molnupiravir and nirmatrelvir are oral antiviral agents that may reduce the risk of hospitalization and deaths if administered early to high-risk subjects. Remdesivir, baricitinib, anti-IL-6 tocilizumab and dexamethasone are frequently used for treatment of patients with respiratory failure. SUMMARY: COVID-19 pandemic progresses relentlessly with substantial morbidity and mortality especially in unvaccinated subjects. Mass COVID-19 vaccinations are the most important measure for control of the COVID-19 pandemic.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35018385
DOI: 10.1101/2022.01.02.22268641


As COVID-19 continues to pose major risk for vulnerable populations including the elderly, immunocompromised, patients with cancer, and those with contraindications to vaccination, novel treatment strategies are urgently needed. SARS-CoV-2 infects target cells via RGD-binding integrins either independently or as a co-receptor with surface receptor angiotensin-converting enzyme 2 (ACE2). We used pan-integrin inhibitor GLPG-0187 to demonstrate blockade of SARS-CoV-2 pseudovirus infection of target cells. Omicron pseudovirus infected normal human small airway epithelial (HSAE) cells significantly less than D614G or Delta variant pseudovirus, and GLPG-0187 effectively blocked SARS-CoV-2 pseudovirus infection in a dose-dependent manner across multiple viral variants. GLPG-0187 inhibited Omicron and Delta pseudovirus infection of HSAE cells more significantly than other variants. Pre-treatment of HSAE cells with MEK inhibitor (MEKi) VS-6766 enhanced inhibition of pseudovirus infection by GLPG-0187. Because integrins activate TGF-beta signaling, we compared plasma levels of active and total TGF-beta in COVID-19+ patients. Plasma TGF-beta1 levels correlated with age, race, and number of medications upon presentation with COVID-19, but not with sex. Total plasma TGF-beta1 levels correlated with activated TGF-beta1 levels. In our preclinical studies, Omicron infection increased lower airway lung cells less efficiently than other COVID-19 variants. Moreover, inhibition of integrin signaling prevents SARS-CoV-2 Delta and Omicron pseudovirus infectivity, and may mitigate COVID-19 severity through decreased TGF-beta1 activation. This therapeutic strategy may be further explored through clinical testing in vulnerable and unvaccinated populations.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35018385
DOI: 10.1101/2022.01.02.22268641


BACKGROUND: The extent to which the reduced risk of severe disease seen with SARS-CoV-2 Omicron is due to a decrease in variant virulence, or higher levels of population immunity, is currently not clear. METHODS: RdRp target delay (RTD) in the Seegene Allplex(TM) 2019-nCoV PCR assay is a proxy marker for the Delta variant. The absence of this proxy marker in the transition period was used to identify suspected Omicron infections. Cox regression was performed for the outcome of hospital admission in those who tested positive for SARS-CoV-2 on the Seegene Allplex(TM) assay from 1 November to 14 December 2021 in the Western Cape Province, South Africa, public sector. Vaccination status and prior diagnosed infection were adjusted for. RESULTS: 150 cases with RTD and 1486 cases without RTD were included. Cases without RTD had a lower hazard of admission (adjusted Hazard Ratio [aHR] of 0.56, 95%CI 0.34-0.91).
Complete vaccination was protective of admission with an aHR of 0.45 (95% CI 0.26-0.77). CONCLUSION: Omicron has resulted in a lower risk of hospital admission, compared to contemporaneous Delta infection, when using the proxy marker of RTD. Under-ascertainment of reinfections with an immune escape variant remains a challenge to accurately assessing variant virulence.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35235826
DOI: 10.1016/j.ijid.2022.02.051


The identification of the Omicron variant (B.1.1.529.1 or BA.1) of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) in Botswana in November 2021(1) immediately raised alarms due to the sheer number of mutations in the spike glycoprotein that could lead to striking antibody evasion. We(2) and others(3-6) recently reported results in this Journal confirming such a concern. Continuing surveillance of Omicron evolution has since revealed the rise in prevalence of two sublineages, BA.1 with an R346K mutation (BA.1+R346K, also known as BA.1.1) and B.1.1.529.2 (BA.2), with the latter containing 8 unique spike mutations while lacking 13 spike mutations found in BA.1. We therefore extended our studies to include antigenic characterization of these new sublineages. Polyclonal sera from patients infected by wild-type SARS-CoV-2 or recipients of current mRNA vaccines showed a substantial loss in neutralizing activity against both BA.1+R346K and BA.2, with drops comparable to that already reported for BA.1(2,3,5,6). These findings indicate that these three sublineages of Omicron are antigenically equidistant from the wild-type SARS-CoV-2 and thus similarly threaten the efficacies of current vaccines. BA.2 also exhibited marked resistance to 17 of 19 neutralizing monoclonal antibodies tested, including S309 (sotrovimab)(7), which had retained appreciable activity against BA.1 and BA.1+R346K(2-4,6). This new finding shows that no authorized monoclonal antibody therapy could adequately cover all sublineages of the Omicron variant, except for the recently authorized LY-CoV1404 (bebtelovimab).

URL: https://www.ncbi.nlm.nih.gov/pubmed/35240676
DOI: 10.1038/s41586-022-04594-4


The reply letter has been put forth in response to the comment made by Karthyayani Priya Satish entitled "India and the COVID-19 Vaccine." The comment was made in context to our published work "Exploring the covid-19 vaccine candidates against SARS-CoV-2 and its variants: where do we stand and where do we go?" The reply letter is concerned with the newer variant of SARS-CoV-2, i.e., Omicron and its impact on severity and vaccine efficacy. Though the variant is mild, as per the reports, the cases are rising at an unprecedented rate that may create havoc on humankind considering shortages of RT-PCR testing and prevailing unequal vaccine distribution and vaccine hesitancy.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35240913
DOI: 10.1080/21645515.2022.2034458


We compared the risk of severe COVID-19 during two periods 2021 and 2022 when Delta and Omicron, respectively, were the dominating virus variants in Scania county, Sweden. We adjusted for differences in sex, age, comorbidities, prior infection and vaccination. Risk of severe disease from Omicron was markedly lower among vaccinated cases. It was also lower among the unvaccinated but remained high (>5%) for older people and middle-aged men with two or more comorbidities. Efforts to increase vaccination uptake should continue.

COVID 19 is the disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2; SC2) which has caused a world-wide pandemic with striking morbidity and mortality. Evaluation of SC2 strains demonstrated impressive genetic variability and many of these viral variants are now defined as variants of concern (VOC) that cause enhanced transmissibility, decreased susceptibility to antibody neutralization or therapeutics and or the ability to induce severe disease. Currently, the del ta (delta) and omicron (o) variants are particularly problematic based on their impressive and unprecedented transmissibility and ability to cause break through infections. The del ta variant also accumulates at high concentrations in host tissues and has caused waves of lethal disease. Because studies from our laboratory have demonstrated that chitinase 3-like-1 (CHI3L1) stimulates ACE2 and Spike (S) priming proteases that mediate SC2 infection, studies were undertaken to determine if interventions that target CHI3L1 are effective inhibitors of SC2 viral variant infection. Here we demonstrate that CHI3L1 augments epithelial cell infection by pseudoviruses that express the alpha, beta, gamma, delta or omicron S proteins and that the CHI3L1 inhibitors anti-CHI3L1 and kasugamycin inhibit epithelial cell infection by these VOC pseudovirus moieties. Thus, CHI3L1 is a universal, VOC-independent therapeutic target in COVID 19.


The new SARS-CoV-2 variant of concern (VOC) Omicron has more than 30 mutations in the receptor binding domain (RBD) of the Spike protein enabling viral escape from antibodies in vaccinated individuals and increased transmissibility1-6. It is unclear how vaccine immunity protects against Omicron infection. Here we show that vaccinated participants at a superspreader event had robust recall response of humoral and preexisting cellular immunity induced by the vaccines, and an emergent de novo T cell response to non-Spike antigens. We compared cases from a Christmas party where 81 of 110 (74%) developed Omicron breakthrough COVID-19, with Delta breakthrough cases and vaccinated non-infected controls. Omicron cases had significantly increased activated SARS-CoV-2 wild type Spike-specific (vaccine) cytotoxic T cells, activated follicular helper (TFH) cells, functional T cell responses, boosted humoral responses, activated anti-Spike plasmablasts and anti-RBD memory B cells compared to controls. Omicron cases had significantly increased de novo memory T cell responses to non-Spike viral antigens compared to Delta breakthrough cases demonstrating development of broad immunity. The rapid release of Spike and RBD-specific IgG+ B cell plasmablasts and memory B cells into circulation suggested affinity maturation of antibodies and that concerted T and B cell immunity may provide durable broad immunity. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.


The 2019 coronavirus disease (COVID-19) pandemic has had devastating impacts on our global health. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus causing COVID-19, has continued to mutate and spread worldwide despite global vaccination efforts. In particular, the Omicron variant, first identified in South Africa in late November 2021, has now overtaken the Delta variant and become the dominant strain worldwide. Compared to the original strain identified in Wuhan, Omicron features 50
genetic mutations, with 15 mutations in the receptor-binding domain (RBD) of the spike protein, which binds to the human angiotensin-converting enzyme 2 (ACE2) receptor for viral entry. However, it is not completely understood how these mutations alter the interaction and binding strength between the Omicron RBD and ACE2. In this study, we used a combined steered molecular dynamics (SMD) simulation and experimental microscale thermophoresis (MST) approach to quantify the interaction between Omicron RBD and ACE2. We report that the Omicron brings an enhanced RBD-ACE2 interface through N501Y, Q493K/R, and T478K mutations; the changes further lead to unique interaction patterns, remnisicng the features of previously dominated variants, Alpha (N501Y) and Delta (L452R and T478K). Our MST data confirmed that the Omicron mutations in RBD are associated with a five-fold higher binding affinity to ACE2 compared to the RBD of the original strain. In conclusion, our result could help explain the Omicron variantaeuros prevalence in human populations, as higher interaction forces or affinity for ACE2 likely promote greater viral binding and internalization, leading to increased infectivity. TOC GRAPHIC:

URL: https://www.ncbi.nlm.nih.gov/pubmed/35118473
DOI: 10.1101/2022.01.24.477633


The SARS-CoV-2 Omicron BA.1 variant is rapidly spreading worldwide, possibly outcompeting the Delta strain. We investigated the empirical serial interval for both variants using contact tracing data. Overall, we observed a shorter serial interval for Omicron compared to Delta, suggesting faster transmission. Furthermore, results indicate a relation between the empirical serial interval and the vaccination status for both the Omicron and the Delta variant. Consequently, with the progression of the vaccination campaign, the reasons for and extent of dominance of Omicron over Delta may need further assessment. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license.

DOI: 10.1101/2022.01.28.22269756


BACKGROUND: Male patients ages 12-17 years have an elevated risk of mRNA vaccination-associated myo/pericarditis. A risk-benefit analysis of first and second doses of mRNA vaccination in adolescent boys by health status and history of SARS-CoV-2 infection has not been performed. METHODS: Using the Vaccine Adverse Event Reporting System (VAERS), we identified BNT162b2 [Pfizer-BioNTech] myo/pericarditis occurrence according to CDC criteria. Main outcomes were as follows: 1) post-vaccination myo/pericarditis crude incidence in adolescents aged 12-15 and 16-17; and 2) two risk-benefit analyses by age, sex, comorbidity, variant and history of infection. RESULTS: Cases of myo/pericarditis (n = 253) included 129 after dose 1 and 124 after dose 2; 86.9% were hospitalized. Incidence per million after dose two in male patients aged 12-15 and 16-17 was 162.2 and 93.0, respectively. Weighing post-vaccination myo/pericarditis against COVID-19 hospitalization during delta, our risk-benefit analysis suggests that among 12-17-year-olds, two-dose vaccination was uniformly favourable only in nonimmune girls with a comorbidity. In boys with prior infection and no comorbidities, even one dose carried more risk than benefit according to international estimates. In the setting of omicron, one dose may be protective in nonimmune children, but dose two does not appear to confer additional benefit at a population level. CONCLUSIONS: Our findings strongly support individualized paediatric COVID-19 vaccination strategies which weigh protection against severe disease vs. risks of vaccine-associated myo/pericarditis. Research is needed into the nature and implications of this adverse effect as well as immunization strategies which reduce harms in this overall low-risk cohort.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35156705
DOI: 10.1111/eci.13759

Emerging severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) variants, especially those of concern, may have an impact on the virus's transmissibility and pathogenicity, as well as diagnostic equipment performance and vaccine effectiveness. Even though the SARS-CoV-2 Delta variant (B.1.617.2) emerged during India's second wave of infections, Delta variants have grown dominant internationally and are still evolving. On November 26, 2021, World Health Organization identified the variant B.1.1.529 as a variant of concern, naming it Omicron, based on evidence that Omicron contains numerous mutations that may influence its behavior. However, the mode of transmission and severity of the Omicron variant remains unknown. We used computational studies to examine the Delta and Omicron variants in this study and found that the Omicron variant had a higher affinity for human angiotensin-converting enzyme 2 (ACE2) than the Delta variant due to a significant number of mutations in the SARS-CoV-2 receptor-binding domain (RBD), indicating a higher potential for transmission. Based on docking studies, the Q493R, N501Y, S371L, S373P, S375F, Q498R, and T478K mutations contribute significantly to high binding affinity with human ACE2. In comparison to the Delta variant, both the entire spike protein and the RBD in Omicron include a high proportion of hydrophobic amino acids such as leucine and phenylalanine. These amino acids are located within the protein's core and are required for structural stability. We observed a disorder-order transition in the Omicron variant between spike protein RBD regions 468-473, and it may be significant in the influence of disordered residues/regions on spike protein stability and binding to ACE2. A future study might investigate the epidemiological and biological consequences of the Omicron variant.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34914115
DOI: 10.1002/jmv.27526


The current fight against COVID-19 is compounded by the Variants of Concern (VoCs), which can diminish the effectiveness of vaccines and potentially increase viral transmission and severity of disease. MVC-COV1901 is a protein subunit vaccine based on the prefusion SARS-CoV-2 spike protein (S-2P) and is adjuvanted with CpG 1018 and aluminum hydroxide. In this study, we used the Delta variant to challenge hamsters inoculated with S-2P from the Wuhan wildtype and the Beta variant in two-dose or three-dose regimens. Two doses of wildtype S-2P followed by the third dose of Beta variant was shown to induce the highest neutralizing antibody titer against live SARS-CoV-2 of the wildtype and all current VoCs, as well as improved neutralization against Omicron variant pseudovirus compared to three doses of wildtype S-2P. All regimens of vaccination were able to protect hamsters from SARS-CoV-2 Delta variant challenge and resulted in reduced lung live virus titer and pathology. Three doses of vaccination also significantly reduced lung viral RNA titer, regardless of whether the wildtype or Beta variant S-2P was used as the third dose. Based on the immunogenicity and viral challenge data, two doses of wildtype S-2P followed by the third dose of Beta variant S-2P induced potent antibody immune responses against the VoCs.

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DOI: 10.1101/2021.09.29.462344

71. **Kupferschmidt K, Vogel G.** Omicron threat remains fuzzy as cases explode. *Science.* 2022;375(6576):9-10. DOI: 10.1126/science.acz9928

URL: https://www.ncbi.nlm.nih.gov/pubmed/34990256
DOI: 10.1126/science.acz9928
The rapid emergence of new SARS-CoV-2 variants raises a number of public health questions including the capability of diagnostic tests to detect new strains, the efficacy of vaccines, and how to map the geographical distribution of variants to better understand patterns of transmission and possible load on healthcare resources. Next-Generation Sequencing (NGS) is the primary method for detecting and tracing the emergence of new variants, but it is expensive, and it can take weeks before sequence data is available in public repositories. Here, we describe a Polymerase Chain Reaction (PCR)-based genotyping approach that is significantly less expensive, accelerates reporting on SARS-CoV-2 variants, and can be implemented in any testing lab performing PCR. Specific Single Nucleotide Polymorphisms (SNPs) and indels are identified that have high positive percent agreement (PPA) and negative percent agreement (NPA) compared to NGS for the major genotypes that circulated in 2021. Using a 48-marker panel, testing on 1,128 retrospective samples yielded a PPA and NPA in the 96.3 to 100% and 99.2 to 100% range, respectively, for the top 10 most prevalent lineages. The effect on PPA and NPA of reducing the number of panel markers was also explored. In addition, with the emergence of Omicron, we also developed an Omicron genotyping panel that distinguishes the Delta and Omicron variants using four (4) highly specific SNPs. Data from testing demonstrates the capability to use the panel to rapidly track the growing prevalence of the Omicron variant in the United States in December 2021. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-ND 4.0 International license.
19, the omicron variant was associated with less severe disease than the delta variant but still resulted in substantial morbidity and mortality. Vaccinated patients admitted to hospital with covid-19 had significantly lower disease severity than unvaccinated patients for all the variants.

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DOI: 10.1136/bmj-2021-069761


URL: https://www.ncbi.nlm.nih.gov/pubmed/35219839
DOI: 10.1016/j.puhe.2022.01.017


The emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B.1.1.529 (Omicron) variant has led to growing concerns of increased transmissibility and escape of both natural and vaccine-induced immunity. In this analysis, sera from adult participants in a phase 2 clinical study (NCT04405076) were tested for neutralizing activity against B.1.1.529 after a 2-dose (100 μg) mRNA-1273 primary vaccination series and after a 50-μg mRNA-1273 booster dose. Results from this preliminary analysis show that 1 month after completing the primary series, mRNA-1273-elicited serum neutralization of B.1.1.529 was below the lower limit of quantification; however, neutralization was observed at 2 weeks after the mRNA-1273 booster dose, although at a reduced level relative to wild-type SARS-CoV-2 (D614G) and lower than that observed against D614G at 1 month after the primary series. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

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DOI: 10.1016/j.ccell.2022.02.012


On November 26, 2021, the B.1.1.529 COVID-19 variant was named as the Omicron variant of concern. Reports of higher transmissibility and potential immune evasion triggered flight bans and heightened health control measures across the world to stem its distribution. Wastewater-based surveillance has demonstrated to be a useful complement for community-based tracking of SARS-CoV-2 variants. Using design principles of our previous assays that detect SARS-CoV-2 variants (Alpha and Delta), here we report two allele-specific RT-qPCR assays that can quantitatively detect the Omicron variant in wastewater and their validation against full length synthetic Omicron RNA. The first simultaneously targets mutations Q493R, G496S and Q498R, and the other targets the deletion at H69-V70 of the spike protein. This method is open-sourced and can be implemented using commercially available RT-qPCR protocols, and would be an important tool for tracking the spread and introduction of the Omicron variant in communities for informed public health responses. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license.

DOI: 10.1101/2021.12.21.21268077

**Background:** The Omicron (B.1.1.529) variant of SARS-CoV-2 has rapidly achieved global dissemination, accounting for most infections in the United States by December 2021. Risk of severe outcomes associated with Omicron infections, as compared to earlier SARS-CoV-2 variants, remains unclear. **Method(s):** We analyzed clinical and epidemiologic data from cases testing positive for SARS-CoV-2 infection within the Kaiser Permanente Southern California healthcare system from November 30, 2021 to January 1, 2022, using S gene target failure (SGTF) as assessed by the ThermoFisher TaqPath ComboKit assay as a proxy for Omicron infection. We fit Cox proportional hazards models to compare time to any hospital admission and hospital admissions associated with new-onset respiratory symptoms, intensive care unit (ICU) admission, mechanical ventilation, and mortality among cases with Omicron and Delta (non-SGTK) variant infections. We fit parametric competing risk models to compare lengths of hospital stay among admitted cases with Omicron and Delta variant infections. **Result(s):** Our analyses included 52,297 cases with SGTF (Omicron) and 16,982 cases with non-SGTK (Delta [B.1.617.2]) infections, respectively. Hospital admissions occurred among 235 (0.5%) and 222 (1.3%) of cases with Omicron and Delta variant infections, respectively. Among cases first tested in outpatient settings, the adjusted hazard ratios for any subsequent hospital admission and symptomatic hospital admission associated with Omicron variant infection were 0.48 (0.36-0.64) and 0.47 (0.35-0.62), respectively. Rates of ICU admission and mortality after an outpatient positive test were 0.26 (0.10-0.73) and 0.09 (0.01-0.75) fold as high among cases with Omicron variant infection as compared to cases with Delta variant infection. Zero cases with Omicron variant infection received mechanical ventilation, as compared to 11 cases with Delta variant infections throughout the period of follow-up (two-sided p<0.001). Median duration of hospital stay was 3.4 (2.8-4.1) days shorter for hospitalized cases with Omicron variant infections as compared to hospitalized patients with Delta variant infections, reflecting a 69.6% (64.0-74.5%) reduction in hospital length of stay.

**Conclusion(s):** During a period with mixed Delta and Omicron variant circulation, SARS-CoV-2 infections with presumed Omicron variant infection were associated with substantially reduced risk of severe clinical endpoints and shorter durations of hospital stay. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

**DOI:** 10.1101/2022.01.11.22269045


Explosively emerging SARS-CoV-2 variants challenge current nomenclature schemes based on genetic diversity and biological significance. Genomic composition-based machine learning methods have recently performed well in identifying phenotype-genotype relationships. We introduced a framework involving dinucleotide (DNT) composition representation (DCR) to parse the general human adaptation of RNA viruses and applied a three-dimensional convolutional neural network (3D CNN) analysis to learn the human adaptation of other existing coronaviruses (CoVs) and predict the adaptation of SARS-CoV-2 variants of concern (VOCs). A markedly separable, linear DCR distribution was observed in two major genes—receptor-binding glycoprotein and RNA-dependent RNA polymerase (RdRp)—of six families of single-stranded (ssRNA) viruses. Additionally, there was a general host-specific distribution of both the spike proteins and RdRps of CoVs. The 3D CNN based on spike DCR predicted a dominant type II adaptation of most Beta, Delta and Omicron VOCs, with high transmissibility and low pathogenicity. Type I adaptation with opposite transmissibility and pathogenicity was predicted for SARS-CoV-2 Alpha VOCs (77%) and Kappa variants of interest (58%). The identified adaptive determinants included D1118H and A570D mutations and local DNTs. Thus, the 3D CNN model based on DCR features predicts SARS-CoV-2, a major type II human adaptation and is qualified to predict variant adaptation in real time, facilitating the risk-assessment of emerging SARS-CoV-2 variants and COVID-19 control.

**DOI:** 10.1093/bib/bbac036

The B.1.1.529/Omicron variant of SARS-CoV-2 was only recently detected in southern Africa, but its subsequent spread has been extensive, both regionally and globally(1). It is expected to become dominant in the coming weeks(2), probably due to enhanced transmissibility. A striking feature of this variant is the large number of spike mutations(3) that pose a threat to the efficacy of current COVID-19 vaccines and antibody therapies(4). This concern is amplified by the findings of our study. Here we found that B.1.1.529 is markedly resistant to neutralization by serum not only from patients who recovered from COVID-19, but also from individuals who were vaccinated with one of the four widely used COVID-19 vaccines. Even serum from individuals who were vaccinated and received a booster dose of mRNA-based vaccines exhibited substantially diminished neutralizing activity against B.1.1.529. By evaluating a panel of monoclonal antibodies against all known epitope clusters on the spike protein, we noted that the activity of 17 out of the 19 antibodies tested were either abolished or impaired, including ones that are currently authorized or approved for use in patients. Moreover, we also identified four new spike mutations (S371L, N440K, G446S and Q493R) that confer greater antibody resistance on B.1.1.529. The Omicron variant presents a serious threat to many existing COVID-19 vaccines and therapies, compelling the development of new interventions that anticipate the evolutionary trajectory of SARS-CoV-2.

81. Liu Y, Rocklov J. The effective reproduction number for the omicron SARS-CoV-2 variant of concern is several times higher than Delta. *J Travel Med*. 2022. DOI: 10.1093/jtm/taac037

Our review found the effective reproduction number and basic reproduction number of the Omicron variant elicited 3.8 and 2.5 times higher transmissibility than the Delta variant respectively. The Omicron variant has an average basic and effective reproduction number of 8.2 and 3.6.


The Omicron variant of concern (VOC), first detected in Italy at the end of November 2021, has since spread rapidly, despite high vaccine coverage in the Italian population, especially in healthcare workers (HCWs). This study describes an outbreak of SARS-CoV-2 Omicron infection in 15 booster-vaccinated HCWs. On 16 December 2021, two HCWs working in the same ward were infected with SARS-CoV-2. The Omicron VOC was suspected due to S gene target failure on molecular testing. Further investigation revealed that 15 (65%) of 23 HCWs attending a social gathering on 13 December were infected with Omicron, as shown by whole-genome sequencing, with a phylogenetic tree suggesting a common source of exposure. Five of these HCWs experienced mild symptoms. A patient with multiple chronic conditions hospitalized in the same ward was also infected by one of the HCWs involved in the outbreak. Despite being booster vaccinated, this patient required ICU treatment. Ten subjects achieved negativity in 10-19 days. The outbreak in booster-vaccinated subjects confirms the high transmissibility and immune evasion of the Omicron VOC. More stringent non-pharmaceutical interventions, administration of booster doses, and genomic surveillance are crucial long-term strategies to mitigate the consequences of the spread of the Omicron VOC.
INTRODUCTION: Coronavirus disease of 2019 (COVID-19) has resulted in millions of cases worldwide. As the pandemic has progressed, the understanding of this disease has evolved. OBJECTIVE: This first in a two-part series on COVID-19 updates provides a focused overview of the presentation and evaluation of COVID-19 for emergency clinicians. DISCUSSION: COVID-19, caused by Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), has resulted in significant morbidity and mortality worldwide. Several variants exist, including a variant of concern known as Delta (B.1.617.2 lineage) and the Omicron variant (B.1.1.529 lineage). The Delta variant is associated with higher infectivity and poor patient outcomes, and the Omicron variant has resulted in a significant increase in infections. While over 80% of patients experience milder symptoms, a significant proportion can be critically ill, including those who are older and those with comorbidities. Upper respiratory symptoms, fever, and changes in taste/smell remain in the most common presenting symptoms. Extrapulmonary complications are numerous and may be severe, including the cardiovascular, neurologic, gastrointestinal, and dermatologic systems. Emergency department evaluation includes focused testing for COVID-19 and assessment of end-organ injury. Imaging may include chest radiography, computed tomography, or ultrasound. Several risk scores may assist in prognostication, including the 4C (Coronavirus Clinical Characterisation Consortium) score, quick COVID Severity Index (qCSI), NEWS2, and the PRIEST score, but these should only supplement and not replace clinical judgment. CONCLUSION: This review provides a focused update of the presentation and evaluation of COVID-19 for emergency clinicians.

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The Omicron SARS-CoV-2 variant of concern (VOC lineage B.1.1.529), which became dominant in many countries during early 2022, includes several subvariants with strikingly different genetic characteristics. Several countries, including Denmark, have observed the two Omicron subvariants: BA.1 and BA.2. In Denmark the latter has rapidly replaced the former as the dominant subvariant. Based on nationwide Danish data, we estimate the transmission dynamics of BA.1 and BA.2 following the spread of Omicron VOC within Danish households in late December 2021 and early January 2022. Among 8,541 primary household cases, of which 2,122 were BA.2, we identified a total of 5,702 secondary infections among 17,945 potential secondary cases during a 1-7 day follow-up period. The secondary attack rate (SAR) was estimated as 29%
Evidence Search Report: EOC211220v011 ESR

and 39% in households infected with Omicron BA.1 and BA.2, respectively. We found BA.2 to be associated with an increased susceptibility of infection for unvaccinated individuals (Odds Ratio (OR) 2.19; 95%-CI 1.58-3.04), fully vaccinated individuals (OR 2.45; 95%-CI 1.77-3.40) and booster-vaccinated individuals (OR 2.99; 95%-CI 2.11-4.24), compared to BA.1. We also found an increased transmissibility from unvaccinated primary cases in BA.2 households when compared to BA.1 households, with an OR of 2.62 (95%-CI 1.96-3.52). The pattern of increased transmissibility in BA.2 households was not observed for fully vaccinated and booster-vaccinated primary cases, where the OR of transmission was below 1 for BA.2 compared to BA.1. We conclude that Omicron BA.2 is inherently substantially more transmissible than BA.1, and that it also possesses immune-evasive properties that further reduce the protective effect of vaccination against infection, but do not increase its transmissibility from vaccinated individuals with breakthrough infections. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license.

DOI: 10.1101/2022.01.28.22270044


BACKGROUND: The B.1.1.529 (omicron) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified on November 25, 2021, in Gauteng province, South Africa. Data regarding the seroprevalence of SARS-CoV-2 IgG in Gauteng before the fourth wave of coronavirus disease 2019 (Covid-19), in which the omicron variant was dominant, are needed. METHODS: We conducted a seroepidemiologic survey from October 22 to December 9, 2021, in Gauteng to determine the seroprevalence of SARS-CoV-2 IgG. Households included in a previous seroepidemiologic survey (conducted from November 2020 to January 2021) were contacted; to account for changes in the survey population, there was a 10% increase in the households contacted, with the use of the same sampling framework. Dried-blood-spot samples were tested for IgG against SARS-CoV-2 spike protein and nucleocapsid protein with the use of quantitative assays. We also evaluated Covid-19 epidemiologic trends in Gauteng, including cases, hospitalizations, recorded deaths, and excess deaths from the start of the pandemic through January 12, 2022. RESULTS: Samples were obtained from 7010 participants, of whom 1319 (18.8%) had received a Covid-19 vaccine. The seroprevalence of SARS-CoV-2 IgG ranged from 56.2% (95% confidence interval [CI], 52.6 to 59.7) among children younger than 12 years of age to 79.7% (95% CI, 77.6 to 81.5) among adults older than 50 years of age. Vaccinated participants were more likely to be seropositive for SARS-CoV-2 than unvaccinated participants (93.1% vs. 68.4%). Epidemiologic data showed that the incidence of SARS-CoV-2 infection increased and subsequently declined more rapidly during the fourth wave than it had during the three previous waves. The incidence of infection was decoupled from the incidences of hospitalization, recorded death, and excess death during the fourth wave, as compared with the proportions seen during previous waves. CONCLUSIONS: Widespread underlying SARS-CoV-2 seropositivity was observed in Gauteng before the omicron-dominant wave of Covid-19. Epidemiologic data showed a decoupling of hospitalizations and deaths from infections while omicron was circulating. (Funded by the Bill and Melinda Gates Foundation.).

URL: https://www.ncbi.nlm.nih.gov/pubmed/35196424
DOI: 10.1056/NEJMoa2119658


Background We conducted a seroepidemiological survey from October 22 to December 9, 2021, in Gauteng Province, South Africa, to determine SARS-CoV-2 immunoglobulin G (IgG) seroprevalence primarily before the fourth wave of coronavirus disease 2019 (Covid-19), in which the B.1.1.529 (Omicron) variant was dominant. We evaluated epidemiological trends in case rates and rates of severe disease through to January 12, 2022, in Gauteng. Methods We contacted households from a previous seroepidemiological survey conducted from November 2020 to January 2021, plus an additional 10% of households using the
same sampling framework. Dry blood spot samples were tested for anti-spike and anti-nucleocapsid protein IgG using quantitative assays on the Luminex platform. Daily case, hospital admission, and reported death data, and weekly excess deaths, were plotted over time. Results: Samples were obtained from 7010 individuals, of whom 1319 (18.8%) had received a Covid-19 vaccine. Overall seroprevalence ranged from 56.2% (95% confidence interval [CI], 52.6 to 59.7) in children aged <12 years to 79.7% (95% CI, 77.6 to 81.5) in individuals aged >50 years. Seropositivity was more likely in vaccinated (93.1%) vs unvaccinated (68.4%) individuals. Epidemiological data showed SARS-CoV-2 infection rates increased and subsequently declined more rapidly than in previous waves. Infection rates were decoupled from Covid-19 hospitalizations, recorded deaths, and excess deaths relative to the previous three waves. Conclusions: Widespread underlying SARS-CoV-2 seropositivity was observed in Gauteng Province before the Omicron-dominant wave. Epidemiological data showed a decoupling of hospitalization and death rates from infection rate during Omicron circulation. Copyright: The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

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SARS-CoV-2 evolution threatens vaccine- and natural infection-derived immunity as well as the efficacy of therapeutic antibodies. To improve public health preparedness, we sought to predict which existing amino acid mutations in SARS-CoV-2 might contribute to future variants of concern. We tested the predictive value of features comprising epidemiology, evolution, immunology, and neural network-based protein sequence modeling, and identified primary biological drivers of SARS-CoV-2 intra-pandemic evolution. We found evidence that ACE2-mediated transmissibility and resistance to population-level host immunity has waxed and waned as a primary driver of SARS-CoV-2 evolution over time. We retroactively identified with high accuracy (area under the receiver operator characteristic curve, AUROC=0.92-0.97) mutations that will spread, at up to four months in advance, across different phases of the pandemic. The behavior of the model was consistent with a plausible causal structure wherein epidemiological covariates combine the effects of diverse and shifting drivers of viral fitness. We applied our model to forecast mutations that will spread in the future and characterize how these mutations affect the binding of therapeutic antibodies. These findings demonstrate that it is possible to forecast the driver mutations that could appear in emerging SARS-CoV-2 variants of concern. We validate this result against Omicron, showing elevated predictive scores for its component mutations prior to emergence, and rapid score increase across daily forecasts during emergence. This modeling approach may be applied to any rapidly evolving pathogens with sufficiently dense genomic surveillance data, such as influenza, and unknown future pandemic viruses.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35014856
DOI: 10.1126/scitranslmed.abk3445


OBJECTIVES: We aimed to investigate the first Omicron cases detected in France in order to assess case characteristics and provide supporting information on the possible impact of this variant on the healthcare system. METHODS: A standardized questionnaire was used to collect information from confirmed and probable Omicron cases. RESULTS: Median age of 468 investigated cases was 35 years, 376 were symptomatic (89%); 64% were vaccinated with two doses and 7% had received three doses. Loss of smell and taste were reported by 8.3% and 9% of cases, respectively. Seven cases were hospitalized, three of those were unvaccinated (including two with reported precondition). No admissions to intensive care and no deaths were reported. CONCLUSIONS: Our results confirm a mild clinical presentation among the first Omicron cases detected in France and highlight the importance for the national COVID-19 surveillance system to quickly detect and adapt to the emergence of a new variant.
90. Mallapaty S. Fourth dose of COVID vaccine offers only slight boost against Omicron infection. *Nature*. 2022. DOI: 10.1038/d41586-022-00486-9

URL: https://www.ncbi.nlm.nih.gov/pubmed/35167979
DOI: 10.1016/j.idnow.2022.02.003


The first U.S. case of COVID-19 attributed to the Omicron variant of SARS-CoV-2 (the virus that causes COVID-19) was reported on December 1, 2021 (1), and by the week ending December 25, 2021, Omicron was the predominant circulating variant in the United States.* Although COVID-19-associated hospitalizations are more frequent among adults,(dagger) COVID-19 can lead to severe outcomes in children and adolescents (2). This report analyzes data from the Coronavirus Disease 19-Associated Hospitalization Surveillance Network (COVID-NET)( section sign) to describe COVID-19-associated hospitalizations among U.S. children (aged 0-11 years) and adolescents (aged 12-17 years) during periods of Delta (July 1-December 18, 2021) and Omicron (December 19, 2021-January 22, 2022) predominance. During the Delta- and Omicron-predominant periods, rates of weekly COVID-19-associated hospitalizations per 100,000 children and adolescents peaked during the weeks ending September 11, 2021, and January 8, 2022, respectively. The Omicron variant peak (7.1 per 100,000) was four times that of the Delta variant peak (1.8), with the largest increase observed among children aged 0-4 years.( paragraph sign) During December 2021, the monthly hospitalization rate among unvaccinated adolescents aged 12-17 years (23.5) was six times that among fully vaccinated adolescents (3.8). Strategies to prevent COVID-19 among children and adolescents, including vaccination of eligible persons, are critical.*.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35176003
DOI: 10.15585/mmwr.mm7107e4


Replication of SARS-CoV-2 in human population is defined by distributions of mutants that are present at different frequencies within the infected host, and can be detected by ultra-deep sequencing techniques. In this study, we have examined the SARS-CoV-2 mutant spectra of amplicons from the spike (S)-coding region of five nasopharyngeal isolates derived from vaccine-breakthrough patients. Interestingly, all patients became infected with the Alpha variant but amino acid substitutions that correspond to the Delta Plus, Iota and Omicron variants were present in the mutant spectra of the resident virus. Deep sequencing analysis of SARS-CoV-2 from vaccine-breakthrough patients revealed a rich reservoir of mutant types, and may also inform of tolerated substitutions that can be represented in epidemiological dominant variants.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35259127
DOI: 10.1172/JCI157700


The Omicron variant features enhanced transmissibility and antibody escape. Here, we describe the Omicron receptor-binding domain (RBD) mutational landscape using amino acid interaction (AAI) networks, which are well suited for interrogating constellations of mutations that function in an epistatic manner. Using AAI, we map Omicron mutations directly and indirectly driving increased escape breadth and depth in
Further, we present epitope networks for authorized therapeutic antibodies and assess perturbations to each antibody's epitope. Since our initial modeling following the identification of Omicron, these predictions have been realized by experimental findings of Omicron neutralization escape from therapeutic antibodies ADG20, AZD8895, and AZD1061. Importantly, the AAI predicted escape resulting from indirect epitope perturbations was not captured by previous sequence or point mutation analyses. Finally, for several Omicron RBD mutations, we find evidence for a plausible role in enhanced transmissibility via disruption of RBD-down conformational stability at the RBDdown-RBDdown interface.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35233548
DOI: 10.1016/j.xcrm.2022.100527


The SARS-CoV-2 Omicron sub-variants BA.1 and BA.2 have become the dominant variants worldwide due to enhanced transmissibility and immune evasion. In response to the rise of BA.1 and BA.2, two recent studies by Liu et al. and Iketani et al. provide a detailed analysis of loss of therapeutic antibody potency through evaluation of escape by pseudotyped viruses harboring BA.1 and BA.2 receptor binding domain (RBD) point mutations. Surprisingly, Liu et al. and Iketani et al. observed a profoundly broad escape effect for the individual mutations S371L and S371F. This result cannot be explained by known escape mechanisms of the SARS-CoV-2 RBD, and conflicts with existing computational and experimental escape measurements for S371 mutations performed on monomeric RBD. Through an examination of these conflicting datasets and a structural analysis of the antibodies assayed by Liu et al. and Iketani et al., we propose a mechanism to explain S371L/F escape according to a perturbation of spike trimer conformational dynamics that has not yet been described for any SARS-CoV-2 escape mutation. The proposed mechanism is relevant to Omicron and future variant surveillance as well as therapeutic antibody design.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35262083
DOI: 10.1101/2022.02.25.481957


Background: Mutations in the receptor binding domain of the SARS-CoV-2 Spike protein are associated with increased transmissibility or substantial reductions in vaccine efficacy, including in the recently described Omicron variant. The changing frequencies of these mutations combined with their differing susceptibility to available therapies have posed significant problems for clinicians and public health professionals. Objective(s): To develop an assay capable of rapidly and accurately identifying variants including Omicron in clinical specimens to enable case tracking and/or selection of appropriate clinical treatment. Study Design: Using three duplex RT-ddPCR reactions targeting four amino acids, we tested 419 positive clinical specimens from February to December 2021 during a period of rapidly shifting variant prevalences and compared genotyping results to genome sequences for each sample, determining the sensitivity and specificity of the assay for each variant. Result(s): Mutation determinations for 99.7% of detected samples agree with NGS data for those samples, and are accurate despite wide variation in RNA concentration and potential confounding factors like transport medium, presence of additional respiratory viruses, and additional mutations in primer and probe sequences. The assay accurately identified the first 15 Omicron variants in our laboratory including the first Omicron in Washington State and discriminated against an S-gene dropout Delta specimen. Conclusion(s): We describe an accurate, precise, and specific RT-ddPCR assay for variant detection that remains robust despite being designed prior to the emergence of Delta and Omicron variants. The assay can quickly identify mutations in current and past SARS-CoV-2 variants, and can be adapted to future mutations. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license.

The ongoing COVID-19 pandemic caused by SARS-CoV-2 is associated with high morbidity and mortality. This zoonotic virus has emerged in Wuhan of China in December 2019 from bats and pangolins probably and continuing the human-to-human transmission globally since last two years. As there is no efficient approved treatment, a number of vaccines were developed at an unprecedented speed to counter the pandemic. Moreover, vaccine hesitancy is observed that may be another possible reason for this never ending pandemic. In the meantime, several variants and mutations were identified and causing multiple waves globally. Now, the safety and efficacy of these vaccines are debatable and recommended to determine whether vaccines are able to interrupt transmission of SARS-CoV-2 variant of concern (VOC). Moreover, the VOCs continue to emerge that appear more transmissible and less sensitive to virus-specific immune responses. In this overview, we have highlighted various drugs and vaccines used to counter this pandemic along with their reported side effects. Moreover, the preliminary data for the novel VOC "Omicron" are discussed with the existing animal models.

**URL:** https://www.ncbi.nlm.nih.gov/pubmed/35184391
**DOI:** 10.1111/cbdd.14035


The COVID-19 pandemic continues to pose a threat to the general population. The ongoing vaccination programs provide protection to individuals and facilitate the opening of society and a return to normalcy. However, emergent and existing SARS-CoV-2 variants capable of evading the immune system endanger the efficacy of the vaccination strategy. To preserve the efficacy of SARS-CoV-2 vaccination globally, aggressive and effective surveillance for known and emerging SARS-CoV-2 Variants of Concern (VOC) is required. Rapid and specific molecular diagnostics can provide speed and coverage advantages compared to genomic sequencing alone, benefitting the public health response and facilitating VOC containment. In this work, we expand the recently developed SARS-CoV-2 CRISPR-Cas detection technology (SHERLOCK) to allow rapid and sensitive discrimination of VOCs, that can be used at point of care and/or implemented in the pipelines of small or large testing facilities, and even determine proportion of VOCs in pooled population-level wastewater samples. This technology aims to complement the ongoing sequencing efforts to allow facile and, crucially, rapid identification of individuals infected with VOCs to help break infection chains. Here, we show the optimisation of our VarLOCK assays (Variant-specific SHERLOCK) for multiple specific mutations in the S gene of SARS-CoV-2 and validation with samples from the Cardiff University Testing Service. We also show the applicability of VarLOCK to national wastewater surveillance of SARS-CoV-2 variants. In addition, we show the rapid adaptability of the technique for new and emerging VOCs such as Omicron. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC 4.0 International license.

**DOI:** 10.1101/2022.01.06.21268555


**Background:** Using classical and genomic epidemiology, we tracked the COVID-19 pandemic in Kenya over 23 months to determine the impact of SARS-CoV-2 variants on its progression. Methods: SARS-CoV-2 surveillance and testing data were obtained from the Kenya Ministry of Health, collected daily from 306 health facilities. COVID-19-associated fatality data were also obtained from these health facilities and
communities. Whole SARS-CoV-2 genome sequencing were carried out on 1241 specimens. Results: Over the pandemic duration (March 2020 - January 2022) Kenya experienced five waves characterized by attack rates (AR) of between 65.4 and 137.6 per 100,000 persons, and in tra-wave case fatality ratios (CFR) averaging 3.5%, two-fold higher than the national average COVID-19 associated CFR. The first two waves that occurred before emergence of global variants of concerns (VoC) had lower AR (65.4 and 118.2 per 100,000). Waves 3, 4, and 5 that occurred during the second year were each dominated by multiple introductions each, of Alpha (74.9% genomes), Delta (98.7%), and Omicron (87.8%) VoCs, respectively. During this phase, government-imposed restrictions failed to alleviate pandemic progression, resulting in higher attack rates spread across the country. Conclusions: The emergence of Alpha, Delta, and Omicron variants was a turning point that resulted in widespread and higher SARS-CoV-2 infections across the country.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35262086
DOI: 10.1101/2022.02.28.22271467

99. Nolan T. Tom Nolan’s research reviews-10 February 2022. BMJ. 2022;376:o325. DOI: 10.1136/bmj.o325
URL: https://www.ncbi.nlm.nih.gov/pubmed/35144929
DOI: 10.1136/bmj.o325


SARS-CoV-2, the causative virus for COVID-19 has now super-mutated into the Omicron (Om) variant. On its spike (S) glycoprotein alone, more than 30 substitutions have been characterized with 15 within the receptor binding domain (RBD); it therefore calls to question the transmissibility and antibody escape capability of Omicron. This study was setup to investigate the Omicron RBD’s interaction with ACE2 (host receptor) and a SARS-CoV-2 neutralizing monoclonal antibody (mAb). In-silico mutagenesis was used to generate the Om-RBD in complex with ACE2 or mAb from the wildtype. HDock server was used to redock and score the mAbs in Om-RBD bound state relative to the wildtype. Stability of interaction between all complexes were investigated using all-atom molecular dynamics (MD). Analyses of trajectories showed that Om-RBD has evolved into an efficient ACE2 binder, via pi-pi (Om-RBD-Y501/ACE2-Y41) and salt-bridge (Om-RBD-K493/ACE2-Y41) interactions. Conversely, in binding mAb, it has become less efficient (Center of mass distance of RBD from mAb complex, wildtype approximately 30 Å, Omicron approximately 41 Å). Disruption of Om-RBD/mAb complex resulted from loose interaction between Om-RBD and the light chain complementarity-determining region residues. Omicron is expected to be better transmissible and less efficiently interacting with neutralizing convalescent mAbs with consequences on transmissibility provided other mutations within the S protein similarly promote cell fusion and viral entry.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35066447
DOI: 10.1016/j.compbiomed.2022.105226


OBJECTIVES: Predictive scores are important tools for the triage of patients with coronavirus disease 2019. The PRIORITY score is advantageous because it does not require laboratory and radiologic information. However, the original development and validation cohorts studied only unvaccinated patients in early 2020. We aimed to externally validate the PRIORITY score in a cohort of patients with the novel delta and omicron variants of coronavirus disease 2019 and mixed vaccination status. METHODS: A total of 410 patients were included in a cross-sectional sampling of all patients admitted to the National Centre of Infectious Diseases on October 27, 2021. A further 102 and 136 patients with vaccine-breakthrough Delta and Omicron variant infection from April to August and December 2021, respectively, were also included.
Variables at the time of admission were collected retrospectively from medical records and used to calculate the probability of deterioration using the PRIORITY model. RESULTS: Of the total 648 included patients, 447 (69.0%) were vaccinated. The mean age was 61.6 years (standard deviation +/- 19.0 years), and 268 patients (41.4%) were female. A total of 112 patients (17.3%) met the primary outcome of developing critical illness or mortality. The performance of the score in this cohort was comparable with the original cohorts, with an area under the receiver operating characteristic curve for all patients of 0.794 (95% CI, 0.752-0.835; p < 0.001), regression coefficient of 1.069, and intercept of 0.04. Subgroup analysis of unvaccinated and vaccinated patients showed that performance was superior in vaccinated individuals, with an area under the receiver operating characteristic curve of 0.684 (95% CI, 0.608-0.760; p < 0.0001) and 0.831 (95% CI, 0.772-0.891; p < 0.0001), respectively. DISCUSSION: Our data support the continued use of the PRIORITY score in this era of novel variants and increased vaccination uptake.

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DOI: 10.1016/j.cmi.2022.01.031


Despite extensive worldwide vaccination, the current COVID-19 pandemic caused by SARS-CoV-2 continues. The Omicron variant is a recently emerged variant of concern and is now taking over the Delta variant. To characterize the potential antigenicity of the Omicron variant, we examined the distributions of SARS-CoV-2 nonself mutations (in reference to the human proteome) as 5 amino acid stretches of short constituent sequences (SCSs) in the Omicron and Delta proteomes. The number of nonself SCSs did not differ much throughout the Omicron, Delta, and Reference Sequence (RefSeq) proteomes but markedly increased in the receptor binding domain (RBD) of the Omicron spike protein compared to those of the Delta and RefSeq proteins. In contrast, the number of nonself SCSs decreased in non-RBD regions in the Omicron spike protein, compensating for the increase in the RBD. Several nonself SCSs were tandemly present in the RBD of the Omicron spike protein, likely as a result of selection for higher binding affinity to the ACE2 receptor (and hence higher infectivity and transmissibility) at the expense of increased antigenicity. Taken together, the present results suggest that the Omicron variant has evolved to have higher antigenicity and less virulence in humans despite increased infectivity and transmissibility. Copyright The copyright holder for this preprint is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license.

DOI: 10.1101/2021.12.30.474613


In this study, a new approach to COVID-19 pandemic is presented. In this context, a fractional order pandemic model is developed to examine the spread of COVID-19 with and without Omicron variant and its relationship with heart attack using real data from the United Kingdom. In the model, heart attack is adopted by considering its relationship with the quarantine strategy. Then, the existence, uniqueness, positivity and boundedness of the solution are studied. The equilibrium points and their stability conditions are achieved. Subsequently, we calculate the basic reproduction number (the virus transmission coefficient) that simply refers to the number of people, to whom an infected person can make infected, as \( R_0 = 3.6456 \) by using the next generation matrix method. Next, we consider the sensitivity analysis of the parameters according to \( R_0 \). In order to determine the values of the parameters in the model, the least squares curve fitting method, which is one of the leading methods in parameter estimation, is benefited. A total of 21 parameter values in the model are estimated by using real Omicron data from the United Kingdom. Moreover, in order to highlight the advantages of using fractional differential equations, applications related to memory trace and hereditary properties are
given. Finally, the numerical simulations are presented to examine the dynamic behavior of the system. As a result of numerical simulations, an increase in the number of people who have heart attacks is observed when Omicron cases were first seen. In the future, it is estimated that the risk of heart attack will decrease as the cases of Omicron decrease.

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DOI: 10.1016/j.choas.2022.111954


URL: https://www.ncbi.nlm.nih.gov/pubmed/34914120
DOI: 10.1002/jmv.27528


At the end of 2021 a new SARS-CoV-2 variant, Omicron, emerged and quickly spread across the world. It has been demonstrated that Omicron’s high number of Spike mutations lead to partial immune evasion from even polyclonal antibody responses, allowing frequent re-infection and vaccine breakthroughs. However, it seems unlikely these antigenic differences alone explain its rapid growth; here we show Omicron replicates rapidly in human primary airway cultures, more so even than the previously dominant variant of concern, Delta. Omicron Spike continues to use human ACE2 as its primary receptor, to which it binds more strongly than other variants. Omicron Spike mediates enhanced entry into cells expressing several different animal ACE2s, including various domestic avian species, horseshoe bats and mice suggesting it has an increased propensity for reverse zoonosis and is more likely than previous variants to establish an animal reservoir of SARS-CoV-2. Unlike other SARS-CoV-2 variants, however, Omicron Spike has a diminished ability to induce syncytia formation. Furthermore, Omicron is capable of efficiently entering cells in a TMPRSS2-independent manner, via the endosomal route. We posit this enables Omicron to infect a greater number of cells in the respiratory epithelium, allowing it to be more infectious at lower exposure doses, and resulting in enhanced intrinsic transmissibility. Copyright The copyright holder for this preprint is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC 4.0 International license.

DOI: 10.1101/2021.12.31.474653


Introduction Early reports showed that Omicron (BA.1) SARS-CoV-2 could be less severe. However, the magnitude of risk reduction of hospitalization and mortality of Omicron (BA.1) infections compared with Delta (B.1.617.2) is not yet clear. This study compares the risk of severe disease among patients infected with the Omicron (BA.1) variant with patients infected with Delta (B.1.617.2) variant in Portugal. Methods We conducted a cohort study in individuals diagnosed with SARS-CoV-2 infection between 1st and 29th December 2021. Cases were individuals with a positive PCR test notified to the national surveillance system. SARS-CoV-2 variants were classified first by whole genomic sequencing (WGS) and, if this information was unavailable, by detecting the S gene target failure. We considered a hospitalization for all the patients admitted within the 14 days after the SARS-CoV-2 infection; after that period, they were censored. The comparison of the risk of hospitalization between Omicron (BA.1) and Delta (B.1.617.2) VOC was estimated using a Cox proportional hazards model. The mean length of stay was compared using linear regression, and the risk of death between Omicron and Delta patients was estimated with a penalized logistic regression. All models were adjusted for sex, age, previous infection, and vaccination...
Background: A correlate of protection (CoP) is an immunological marker associated with protection against infection. A CoP can be used to determine whether an individual is protected from infection, evaluate candidate vaccines, guide vaccination dosing intervals and policy, and understand population-level immunity against a pathogen. Despite an urgent need, a CoP for SARS-CoV-2 is currently undefined, leaving an evidence gap for informing public health policy and adapting it appropriately as new variants of concern emerge. The objective of this study was to systematically review and assess the evidence for a humoral SARS-CoV-2 CoP.

Methods and Findings: We searched OVID MEDLINE, EMBASE, Global Health, BIOSIS Previews and Scopus from inception to December 31, 2021, for studies describing SARS-CoV-2 immunity of participants who had received a two-dose regimen of CoronaVac, an inactivated vaccine used globally. We found that a heterologous CoronaVac prime vaccination of two doses followed by a BNT162b2 booster induces elevated virus-specific antibody levels and potent neutralization activity against the ancestral virus and the Delta variant, resembling the titers obtained after two doses of mRNA vaccines. Although neutralization of Omicron was undetectable in participants who had received a two-dose regimen of CoronaVac, the BNT162b2 booster resulted in a 1.4-fold increase in neutralization activity against Omicron compared with the two-dose mRNA vaccine. Despite this increase, neutralizing antibody titers were reduced by 7.1-fold and 3.6-fold for Omicron compared with the ancestral strain and the Delta variant, respectively. These findings have immediate implications for multiple countries that previously used a CoronaVac regimen and reinforce the idea that the Omicron variant is associated with immune escape from vaccines or infection-induced immunity, highlighting the global need for vaccine boosters to combat the impact of emerging variants.


URL: https://www.ncbi.nlm.nih.gov/pubmed/35051990
DOI: 10.1038/s41591-022-01705-6


Background: A correlate of protection (CoP) is an immunological marker associated with protection against infection. A CoP can be used to determine whether an individual is protected from infection, evaluate candidate vaccines, guide vaccination dosing intervals and policy, and understand population-level immunity against a pathogen. Despite an urgent need, a CoP for SARS-CoV-2 is currently undefined, leaving an evidence gap for informing public health policy and adapting it appropriately as new variants of concern emerge. The objective of this study was to systematically review and assess the evidence for a humoral SARS-CoV-2 CoP.

Methods and Findings: We searched OVID MEDLINE, EMBASE, Global Health, BIOSIS Previews and Scopus from inception to January 4, 2022 and pre-prints (using NIH iSearch COVID-19 portfolio) from inception to December 31, 2021, for studies describing SARS-CoV-2 re-infection or breakthrough infection with associated antibody measures. Two reviewers independently extracted study data and performed quality assessment. Twenty-five studies were included in our systematic review. Several studies reported re-infection or breakthrough cases that occurred in the presence of robust antibody levels. Studies that compared aggregate antibody concentrations from individuals who experienced reinfection or breakthrough compared to those who remained protected did not always find
differences that were statistically significant. However, several studies found an inverse relationship between antibody levels and infection incidence, risk, or viral load, and a correlation between antibody levels and vaccine efficacy (VE). Estimates of the contribution of antibody levels to VE varied from 48.5% to 94.2%, suggesting that both humoral immunity and other immune components contribute to protection. Only two studies estimated a quantitative CoP. For Ancestral SARS-CoV-2, these included 154 (95% confidence interval (CI) 42, 559) anti-S binding antibody units/mL (BAU/mL), and 28.6% (95% CI 19.2, 29.2%) of the mean convalescent antibody level following infection. One study reported a CoP for the Alpha (B.1.1.7) variant of concern of 171 (95% CI 57, 519) BAU/mL. As of our search date, no studies reported an Omicron-specific CoP. Conclusion(s): The reviewed literature was limited by a wide variation in assay methodology and antibody targets. Few studies reported SARS-CoV-2 lineage. The studies included in our review suggest that if it exists, a SARS-CoV-2 CoP is likely relative, where higher antibody levels decrease the risk of infection, but do not eliminate it completely. More work is urgently needed in this area to establish a SARS-CoV-2 CoP and guide policy as the pandemic continues.

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DOI: 10.1101/2022.01.21.22269667


The Omicron variant of SARS-CoV-2 is transmissible in vaccinated and unvaccinated populations. Here, we describe the rapid dominance of Omicron following its introduction to three Massachusetts universities with asymptomatic surveillance programs. We find that Omicron was established and reached fixation earlier on these campuses than in Massachusetts or New England as a whole, rapidly outcompeting Delta despite its association with lower viral loads. These findings highlight the transmissibility of Omicron and its propensity to fixate in small populations, as well as the ability of robust asymptomatic surveillance programs to offer early insights into the dynamics of pathogen arrival and spread. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC-ND 4.0 International license.

DOI: 10.1101/2022.01.27.22269787


The first case of the new SARS-CoV-2 Omicron Variant of Concern (VOC) from South Africa was reported to WHO on November 24, 2021....

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DOI: 10.1128/jcm.00024-22


Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the causative agent of coronavirus disease-19 (Covid-19) which has been designated a worldwide pandemic by the World Health Organization on March 11, 2020. Since that time, the virus has mutated and an assortment of variants have been successful at establishing themselves in the human population. This review article describes the SARS-CoV-2 genome, hot spot mutations, variants, and then focuses on the Delta variant, finishing up with an update on the Omicron variant. The genome encompasses 11 open reading frames, one of which encodes the spike or S protein that has been the target for vaccines and some of the drugs because of its role in attachment to the human host cell, as well as antibodies. Mutations in the S protein that are common among several of the variants include D614G that increases transmissibility and viral load and is often associated with P323L on the RNA dependent RNA polymerase. N501Y is a mutation in the receptor binding domain of the S
protein that increases binding to the ACE-2 receptor on the human host cells by 10 fold. The discussed variants carry combinations of these and other mutations and are classified by the World Health Organization as variants of concern, variants of interest, and variants under monitoring. All variants are characterized by increased transmissibility (relative to the original SARS CoV-2), which is the reason for their ability to establish themselves. Several but not all variants are more resistant to antiviral drugs and less susceptible to antibodies/vaccines. The Delta variant that dominated the world until November 2021 causes an increased risk for hospitalization and death, but is still very susceptible to the current vaccines. The most recent variant, Omicron, is characterized by increased transmissibility and decreased antibody susceptibility.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35227008
DOI: 10.31083/j.fbl2702065

112. Quilty BJ, Pulliam JRC, Pearson CAB. Test to release from isolation after testing positive for SARS-CoV-2. medRxiv. 2022. DOI: 10.1101/2022.01.04.21268372

The rapid spread and high transmissibility of the Omicron variant of SARS-CoV-2 is likely to lead to a significant number of key workers testing positive simultaneously. Under a policy of self-isolation after testing positive, this may lead to extreme staffing shortfalls at the same time as e.g. hospital admissions are peaking. Using a model of individual infectiousness and testing with lateral flow tests (LFT), we evaluate test-to-release policies against conventional fixed-duration isolation policies in terms of excess days of infectiousness, days saved, and tests used. We find that the number of infectious days in the community can be reduced to almost zero by requiring at least 2 consecutive days of negative tests, regardless of the number of days' wait until testing again after initially testing positive. On average, a policy of fewer days' wait until initiating testing (e.g. 3 or 5 days) results in more days saved vs. a 10-day isolation period, but also requires a greater number of tests. Due to a lack of specific data on viral load progression, infectivity, and likelihood of testing positive by LFT over the course of an Omicron infection, we assume the same parameters as for pre-Omicron variants and explore the impact of a possible shorter proliferation phase. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC-ND 4.0 International license.

DOI: 10.1101/2022.01.04.21268372


The Coronavirus Disease-2019 (COVID-19) pandemic is still challenging public health systems worldwide, particularly with the emergence of novel SARS-CoV-2 variants with mutations that increase their transmissibility and immune escape. This is the case of the Variant of Concern (VOC) Omicron that rapidly spread globally. Here, using epidemiological and genomic data we compared the situations in South Africa as the epicenter of emergence, United Kingdom, and with particular interest New York city. This rapid global dispersal from the place of first report reemphasizes the high transmissibility of Omicron, which needed only two weeks to become dominant in the UK and NYC. Our analyses suggest that as SARS-CoV-2 continues to evolve, global authorities must prioritize equity in vaccine access and continued genomic surveillance. Future studies are still needed to fully unveil the biological properties of Omicron, but what is certain is that vaccination, large-scale testing, and infection prevention efforts are the greatest arsenal against the COVID-19 pandemic. This article is protected by copyright. All rights reserved.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35243662
DOI: 10.1002/jmv.27691

The Omicron variant of coronavirus has caused major disruptions worldwide with countries struggling to manage the overwhelming number of infections. Omicron is found to be significantly more transmissible compared to its predecessors and therefore almost every impacted country is exhibiting new infection peaks than seen earlier. In this work, we analyze the global statistics of Omicron-impacted countries including South Africa, the United Kingdom, the United States, France, and Italy to quantitatively estimate the intensity and severity of recent waves. Next, these statistics are used to estimate the impact of Omicron in India, which is experiencing an intense third wave of COVID-19 since 28 Dec., 2021. The rapid surge in the daily number of infections, comparable to the global trends, strongly suggests the dominance of the Omicron variant in infections in India. The logarithmic regression suggests the early growth rate of infections in this wave is nearly four times that in the second wave. Another notable difference in this wave is the relatively concurrent arrival of outbreaks all across the country; the effective reproduction number (Rt) although has significant variations among different regions. The test positivity rate (TPR) also displays a rapid growth in the last 10 days in several states. Preliminary estimates with the Susceptible-Infected-Removed (SIR) model suggest that the peak in India to occur in late January 2022 with a caseload exceeding that in the second wave. Although global Omicron trends, as analyzed in this work, suggest a decline in case fatality rate and hospitalizations compared to Delta, a sudden accumulation of active infections can potentially choke the already stressed healthcare infrastructure for the next few weeks. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC 4.0 International license.

DOI: 10.1101/2022.01.09.22268969

As severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) evolves, it accumulates mutations, which are changes in the genetic code. Because this virus has built-in RNA repair mechanisms, it generates mutations more slowly than some other RNA viruses. Thousands of mutations have emerged since the beginning of the pandemic throughout all virus genomes sequenced to date, resulting in thousands of distinct variants. However, some variants have recently been discovered that appear to increase transmissibility and may affect illness pervasiveness. In this study, we investigated SARS-CoV-2 variants and how countries intervene with them. We also depicted the top 25 countries where the Omicron variant is prevalent, with the UK, US, Denmark, France, and Australia having the top five places as of January 13, 2022. The perception of SARS-CoV-2 variants was investigated in those five countries, and the propagation rate of the Omicron variant was determined to be 51%, 29%, 26%, 15%, and 44%, respectively, indicating that the Omicron variant is the most prevalent among the others. Then, a study of SARS-CoV-2 infection test rate based on tests conducted per one million populations with a number of sequences in those five countries reveals that 25%, 73%, 1.6%, 4.8%, and 1.5%, respectively, it suggests that viral testing should be increased in all five countries since it will help to determine the precise distribution of variants and aid governments in making policy decisions for public safety. We anticipated the production of new variants strains. This study implies that limiting disease transmissions, such as acquiring a coronavirus disease 2019 vaccine and booster doses for those aged 18 and older, as well as wearing the mask in public places, is the best strategy to prevent the emergence of new variants.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35112734
DOI: 10.1002/jmv.27634

There is a growing concern that ongoing evolution of SARS-CoV-2 could lead to variants of concern (VOC) that are capable of avoiding some or all of the multifaceted immune response generated by both prior infection or vaccination, with the recently described B.1.1.529 (Omicron) VOC being of particular interest. Peripheral
Evidence Search Report: EOC211220v011 ESR


**Background:** The COVID-19 pandemic situation has been changing drastically worldwide due to the continuous appearance of SARS-CoV-2 variants and the roll-out of mass vaccination. Periodic cross-sectional studies during the surge of COVID-19 cases is essential to elucidate the pandemic situation. **Method(s):** Sera of 1,000 individuals who underwent a health check-up in Hyogo Prefecture Health Promotion Association clinics in Japan were collected in August and December 2021. Antibodies against SARS-CoV-2 N and S antigens were detected in the sera by an electrochemiluminescence immunoassay (ECLIA) and an enzyme-linked immunosorbent assay (ELISA), respectively. The sera’s neutralization activities for the conventional SARS-CoV-2 (D614G), Delta, and Omicron variants were measured. **Result(s):** The seropositive rates for the antibody against N antigen were 2.1% and 3.9% in August and December 2021 respectively, demonstrating a Delta variant endemic during that time; the actual infection rate was approximately twofold higher than the rate estimated based on the polymerase chain reaction (PCR)-based diagnosis. The anti-S seropositive rate was 38.7% in August and it reached 90.8% in December, in concordance with the vaccination rate in Japan. In the December cohort, 78.7% of the sera showed neutralizing activity against the Delta variant, whereas that against the Omicron was much lower at 36.6%. **Conclusion(s):** These analyses revealed that herd immunity against SARS-CoV-2 including the Delta variant was established in December 2021, leading to convergence of the variants. The low neutralizing activity against the Omicron variant suggests the need for the further promotion of the prompt three-dose vaccination to overcome this variant’s imminent 6th wave in Japan.Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

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The aim of the present paper is to highlight that new variants, either of higher viral load such as delta or higher contagiousness like omicron, lead to an even higher airborne transmission than historical strains. We first review the question of the route of contamination and of the dose following exposure, and the importance of the counting unit for pathogens, itself linked to the dose-response law. Using the counting unit of Wells, i.e. the quantum of contagium, we develop the conservation equation of quanta which allows deriving the value of the quantum concentration at steady state for a well-mixed room. With the choice of an exponential response function, this leads to the famous Wells-Riley equation. The analysis points out the importance of a number of parameters such as the time of exposure, the quantum production rate, mask wearing and the incidence rate in the population in order to evaluate the risk. The link with the monitoring concentration of carbon dioxide is made and used for a risk analysis of a variety of situations for which we have made concrete CO2 time monitoring. The main conclusion of these observations is that the present norms of ventilation, already insufficient, are not respected, especially in a variety of public premises, leading to high risk of contamination. Finally, we insist that public health policy in the field of airborne transmission should be based on a multi parameter analysis, considering the whole complexity of dose evaluation.

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Higher COVID-19 incidence and mortality rates in rural than in urban areas are well documented (1). These disparities persisted during the B.1.617.2 (Delta) and B.1.1.529 (Omicron) variant surges during late 2021 and early 2022 (1,2). Rural populations tend to be older (aged >/=65 years) and uninsured and are more likely to have underlying medical conditions and live farther from facilities that provide tertiary medical care, placing them at higher risk for adverse COVID-19 outcomes (2). To better understand COVID-19 vaccination disparities between urban and rural populations, CDC analyzed county-level vaccine administration data among persons aged >/=5 years who received their first dose of either the BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) COVID-19 vaccine or a single dose of the Ad.26.COV2.S (Janssen [Johnson & Johnson]) COVID-19 vaccine during December 14, 2020-January 31, 2022, in 50 states and the District of Columbia (DC). COVID-19 vaccination coverage with >/=1 doses in rural areas (58.5%) was lower than that in urban counties (75.4%) overall, with similar patterns across age groups and sex. Coverage with >/=1 doses varied among states: 46 states had higher coverage in urban than in rural counties, one had higher coverage in rural than in urban counties. Three states and DC had no rural counties; thus, urban-rural differences could not be assessed. COVID-19 vaccine primary series completion was higher in urban than in rural counties. However, receipt of booster or additional doses among primary series recipients was similarly low between urban and rural counties. Compared with estimates from a previous study of vaccine coverage among adults aged >/=18 years during December 14, 2020-April 10, 2021, these urban-rural disparities among those now eligible for vaccination (aged >/=5 years) have increased more than twofold through January 2022, despite increased availability and access to COVID-19 vaccines. Addressing barriers to vaccination in rural areas is critical to achieving vaccine equity, reducing disparities, and decreasing COVID-19-related illness and death in the United States (2).

Background: Solid organ transplant recipients (SOTR), who typically receive post-transplant immunosuppression, show increased COVID-19-related mortality. It is unclear whether an additional dose of COVID-19 vaccines in SOTR can overcome the reduced immune responsiveness against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) variants. Method(s): We performed a prospective cohort study of 53 SOTR receiving SARS-CoV-2 vaccination into a prospective cohort study performing detailed immunoprofiling of humoral immune responses against SARS-CoV-2 and its variants. Result(s): Prior to the additional vaccine dose, 60.3% of SOTR showed no measurable neutralization and only 18.9% demonstrated neutralizing activity of >90% following two vaccine doses. More intensive immunosuppression, antimetabolites in particular, negatively impacted antiviral immunity. While absolute IgG levels were lower in SOTR than controls, antibody titers against microbial recall antigens were in fact higher. In contrast, SOTR showed reduced vaccine-induced IgG/IgA antibody titers against SARS-CoV-2 and its delta variants. Vaccinated SOTR showed a markedly fewer linear B cell epitopes, indicating reduced B cell diversity. Importantly, a third vaccine dose led to an increase in anti-SARS-CoV-2 antibody titers and neutralizing activity across alpha, beta and delta variants. However, we observed a significant decrease in anti-spike antibody titers with the omicron variant. Conclusion(s): Only a small subgroup of SOTR generated functionally relevant antibodies after completing the initial vaccine series based on dysfunctional priming of immune responses against novel antigens. An additional dose of the vaccine results in dramatically improved antibody responses against all SARS-CoV-2 variants except omicron. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

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During November 19-21, 2021, an indoor convention (event) in New York City (NYC), was attended by approximately 53,000 persons from 52 U.S. jurisdictions and 30 foreign countries. In-person registration for the event began on November 18, 2021. The venue was equipped with high efficiency particulate air (HEPA) filtration, and attendees were required to wear a mask indoors and have documented receipt of at least 1 dose of a COVID-19 vaccine.* On December 2, 2021, the Minnesota Department of Health reported the first case of community-acquired COVID-19 in the United States caused by the SARS-CoV-2 B.1.1.529 (Omicron) variant in a person who had attended the event (1). CDC collaborated with state and local health departments to assess event-associated COVID-19 cases and potential exposures among U.S.-based attendees using data from COVID-19 surveillance systems and an anonymous online attendee survey. Among 34,541 attendees with available contact information, surveillance data identified test results for 4,560, including 119 (2.6%) persons from 16 jurisdictions with positive SARS-CoV-2 test results. Most (4,041 [95.2%]), survey respondents reported always wearing a mask while indoors at the event. Compared with test-negative respondents, test-positive respondents were more likely to report attending bars, karaoke, or nightclubs, and eating or drinking indoors near others for at least 15 minutes. Among 4,560 attendees who received testing, evidence of widespread transmission during the event was not identified. Genomic sequencing of 20 specimens identified the SARS-CoV-2 B.1.617.2 (Delta) variant (AY.25 and AY.103 sublineages) in 15 (75%) cases, and the Omicron variant (BA.1 sublineage) in five (25%) cases. These findings reinforce the importance of implementing multiple, simultaneous prevention measures, such as ensuring up-to-date vaccination, mask use, physical distancing, and improved ventilation in limiting SARS-CoV-2 transmission, during large, indoor events.(dagger).

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As the latest identified novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant of concern (VOC), the influence of Omicron on our globe grows promptly. Compared with the last VOC (Delta variant), more mutations were identified, which may address the characteristics of Omicron. Considering these crucial mutations and their implications including an increase in transmissibility, COVID-19 severity, and reduction of efficacy of currently available diagnostics, vaccines, and therapeutics, Omicron has been classified as one of the VOC. Notably, 15 of these mutations reside in the receptor-binding domain of spike glycoprotein, which may alter transmissibility, infectivity, neutralizing antibody escape, and vaccine breakthrough cases of COVID-19. Therefore, our present study characterizes the mutational hotspots of the Omicron variant in comparison with the Delta variant of SARS-CoV-2. Furthermore, detailed information was analyzed to characterize the global perspective of Omicron, including transmission dynamic, effect on testing, and immunity, which shall promote the progress of the clinical application and basic research. Collectively, our data suggest that due to continuous variation in the spike glycoprotein sequences, the use of coronavirus-specific attachment inhibitors may not be the current choice of therapy for emerging SARS-CoV-2 VOCs. Hence, we need to proceed with a sense of urgency in this matter.

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Adopting an early doubling time of three days for the rate of new infections with the omicron mutant the temporal evolution of the omicron wave in different countries is predicted. The predictions are based on the susceptible-infectious-recovered/removed (SIR) epidemic compartment model with a constant stationary ratio $k = \frac{\mu(t)}{a(t)}$ between the infection ($a(t)$) and recovery ($\mu(t)$) rate. The fixed early doubling time then uniquely relates the initial infection rate $a_0$ to the ratio $k$, which therefore determines the full temporal evolution of the omicron waves. For each country three scenarios (optimistic, pessimistic, intermediate) are considered and the resulting pandemic parameters are calculated. These include the total number of infected persons, the maximum rate of new infections, the peak time and the maximum 7-day incidence per 100000 persons. Among the considered European countries Denmark has the smallest omicron peak time and the recently observed saturation of the 7-day incidence value at 2478 is in excellent agreement with the prediction in the optimistic scenario. For Germany we predict peak times of the omicron wave ranging from 32 to 38 and 45 days after the start of the omicron wave in the optimistic, intermediate and pessimistic scenario, respectively, with corresponding maximum SDI values of 7090, 13263 and 28911, respectively. Adopting Jan 1st, 2022 as the starting date our predictions implies that the maximum of the omicron wave is reached between Feb 1 and Feb 15, 2022. Rather similar values are predicted for Switzerland. Due to an order of magnitude smaller omicron hospitalization rate, due to the high percentage of vaccinated and boostered population, the German health system can cope with maximum omicron SDI value of 2800 which is about a factor 2.5 smaller than the maximum omicron SDI value 7090 in the optimistic case. By either reducing the duration of intensive care during this period of maximum, and/or by making use of the nonuniform spread of the omicron wave across Germany, it seems that the German health system can barely cope with the omicron wave avoiding triage decisions. The reduced omicron hospitalization rate also causes significantly smaller mortality rates compared to the earlier mutants in Germany. In the optimistic scenario one obtains for the total number of fatalities 7445 and for the maximum death rate 418 per day which are about one order of magnitude smaller than the beta fatality rate and total number. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC-ND 4.0 International license.

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Effective vaccines and monoclonal antibodies have been developed against coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, the appearance of virus variants with higher transmissibility and pathogenicity is a major concern because of their potential to escape vaccines and clinically approved SARS-CoV-2 antibodies. Here, we use flow cytometry-based binding and pseudotyped SARS-CoV-2 neutralization assays to determine the efficacy of boost immunization and therapeutic antibodies to neutralize the dominant Omicron variant. We provide compelling evidence that the third vaccination with BNT162b2 increases the amount of neutralizing serum antibodies against Delta and Omicron variants, albeit to a lower degree when compared to the parental Wuhan strain. Therefore, a third vaccination is warranted to increase titers of protective serum antibodies, especially in the case of the Omicron variant. We also found that most clinically approved and otherwise potent therapeutic antibodies against the Delta variant failed to recognize and neutralize the Omicron variant. In contrast, some antibodies under pre-clinical development potently neutralized the Omicron variant. Our studies also support using a flow cytometry-based antibody binding assay to rapidly monitor therapeutic candidates and serum titers against emerging SARS-CoV-2 variants. This article is protected by copyright. All rights reserved.

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Virus-like particle (VLP) and live virus assays were used to investigate neutralizing immunity to Delta and Omicron SARS-CoV-2 variants in 239 samples from 125 fully vaccinated individuals. In uninfected, non-boosted individuals, VLP neutralization titers to Delta and Omicron were reduced 2.7-fold and 15.4-fold, respectively, compared to wild-type (WT), while boosted individuals (n=23) had 18-fold increased titers. Delta breakthrough infections (n=39) had 57-fold and 3.1-fold titers whereas Omicron breakthrough infections (n=14) had 5.8-fold and 0.32-fold titers compared to uninfected non-boosted and boosted individuals, respectively. The difference in titers (p=0.049) was related to a higher proportion of moderate to severe infections in the Delta cohort (p=0.014). Correlation of neutralizing and spike quantitative antibody titers was decreased with Delta or Omicron compared to WT. Neutralizing antibodies in Delta and Omicron breakthrough infections increased overall, but the relative magnitude of increase is greater in more clinically severe infection and against the specific infecting variant. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC-ND 4.0 International license.

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In 2019, the world faced a serious health challenge, the rapid spreading of a life-threatening viral pneumonia, coronavirus disease 2019 (COVID-19) caused by a beta coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of January 2022 WHO statistics shows more than 5.6 million death and about 350 million infection by SARS-CoV-2. One of the life threatening aspects of COVID-19 is secondary infections and reduced efficacy of antibiotics against them. Since the beginning of COVID-19 many researches have been done on identification, treatment, and vaccine development. Bacterial viruses (bacteriophages) could offer novel approaches to detect, treat and control COVID-19. Phage therapy and in particular using phage cocktails can be used to control or eliminate the bacterial pathogen as an alternative or complementary therapeutic agent. At the same time, phage interaction with the host immune system can regulate the inflammatory response. In addition, phage display and engineered synthetic phages can be utilized to develop new vaccines and antibodies, stimulate the immune system,
and elicit a rapid and well-appropriate defense response. The emergence of SARS-CoV-2 new variants like delta and omicron has proved the urgent need for precise, efficient and novel approaches for vaccine development and virus detection techniques in which bacteriophages may be one of the plausible solutions. Therefore, phages with similar morphology and/or genetic content to that of coronaviruses can be used for ecological and epidemiological modeling of SARS-CoV-2 behavior and future generations of coronavirus, and in general new viral pathogens. This article is a comprehensive review/perspective of potential applications of bacteriophages in the fight against the present pandemic and the post-COVID era.

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DOI: 10.1016/j.micpath.2022.105442


URL: https://www.ncbi.nlm.nih.gov/pubmed/34927270
DOI: 10.1002/jmv.27532

129. Sidik SM. Had Omicron? You’re unlikely to catch its rising variant. *Nature.* 2022. DOI: 10.1038/d41586-022-00558-w

URL: https://www.ncbi.nlm.nih.gov/pubmed/35217841
DOI: 10.1038/d41586-022-00558-w


Multiple variants of SARS-CoV-2 have emerged and are now prevalent at the global level. Currently designated variants of concern (VOCs) are B.1.1.7, B1.351, P.1, B.1.617.2 variants and B.1.1.529. Possible options for VOC are urgently required as they carry mutations in the virus spike protein that allow them to spread more easily and cause more serious illness. The primary targets for most therapeutic methods against SARS-CoV-2 are the S (Spike) protein and RBD (Receptor-Binding Domain), which alter the binding to ACE2 (Angiotensin-Converting Enzyme 2). The most popular of these strategies involves the use of drug development targeting the RBD and the NTD (N-terminal domain) of the spike protein and multiple epitopes of the S protein. Various types of mutations have been observed in the RBDs of B.1.1.7, B1.351, P. and B.1.620. The incidence of RBD mutations increases the binding affinity to the ACE2 receptor. The high binding affinity of RBD and ACE2 has provided a structural basis for future evaluation of antibodies and drug development. Here we discuss the variants of SARS-CoV-2 and recent updates on the clinical evaluation of antibody-based treatment options. Presently, most of the antibody-based treatments have been effective in patients with SARS-CoV-2. However, there are still significant challenges in verifying independence, and the need for further clinical evaluation.

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On December 2, 2021, the Minnesota Department of Health (MDH) notified CDC of a COVID-19 case caused by sequence-confirmed SARS-CoV-2 B.1.1.529 (Omicron) variant in a Minnesota resident (patient A), the first such case identified in the state and one of the earliest identified in the United States. Patient A had attended a large indoor convention in New York, New York with approximately 53,000 attendees from 52 U.S jurisdictions and 30 foreign countries during November 19-21, 2021, and had close contact (dagger)
Countries continue to debate the need for decontamination of cold-chain food packaging to reduce possible severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) fomite transmission among frontline workers. While laboratory-based studies demonstrate persistence of SARS-CoV-2 on surfaces, the likelihood of fomite-mediated transmission under real-life conditions is uncertain. Using a quantitative microbial risk assessment model of a frozen food packaging facility, we simulated 1) SARS-CoV-2 fomite-mediated infection risks following worker exposure to contaminated plastic packaging; and 2) reductions in these risks from masking, handwashing, and vaccination. In a frozen food facility without interventions, SARS-CoV-2 infection risk to a susceptible worker from contact with contaminated packaging was $1.5 \times 10^{-6}$ per 1h-period (5th - 95th percentile: $9.2 \times 10^{-6}$, $1.2 \times 10^{-5}$). Standard food industry infection control interventions, handwashing and masking, reduced risk (99.4%) to $8.5 \times 10^{-7}$ risk per 1h-period (5th - 95th percentile: $2.8 \times 10^{-8}$, $6.6 \times 10^{-9}$). Vaccination of the susceptible worker (two doses Pfizer/Moderna, vaccine efficacy: 86-99%) with handwashing and masking reduced risk to $5.2 \times 10^{-7}$ risk per 1h-period (5th - 95th percentile: $1.8 \times 10^{-9}$, $5.4 \times 10^{-10}$). Simulating increased transmissibility of current and future variants (Delta, Omicron), (2-, 10-fold viral shedding) among a fully vaccinated workforce, handwashing and masking continued to mitigate risk ($1.4 \times 10^{-6}$ - $8.8 \times 10^{-6}$ risk per 1h-period). Additional decontamination of frozen food plastic packaging reduced infection risks to $1.2 \times 10^{-8}$ risk per 1h-period (5th - 95th percentile: $1.9 \times 10^{-11}$, $9.5 \times 10^{-8}$). Given that standard infection control interventions reduced risks well below $1 \times 10^{-4}$ (World Health Organization water quality risk thresholds), additional packaging decontamination suggest no marginal benefit in risk reduction. Consequences of this decontamination may include increased chemical exposures to workers, food quality and hazard risks to consumers, and unnecessary added costs to governments and the global food industry.

We analysed 131,478 SARS-CoV-2 variant screening tests performed in France from September 1st to December 18, 2021. Tests consistent with the presence of the Omicron variant exhibit significantly higher cycle threshold Ct values, which could indicate lower amounts of virus genetic material. We estimate that the transmission advantage of the Omicron variant over the Delta variant is +105% (95% confidence interval: 96-114%). Based on these data, we use mechanistic mathematical modelling to explore scenarios for early 2022. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

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To clarify transmissibility of the severe acute respiratory syndrome coronavirus 2 Omicron variant, we determined serial intervals and secondary attack rates among household contacts in South Korea. Mean serial interval for 12 transmission pairs was 2.9 days, and secondary attack rate among 25 households was 50.0%, raising concern about a rapid surge in cases.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35107418
DOI: 10.3201/eid2803.212607

135. Spiers N. Recognising and bearing the burden of long COVID-related disability. Br J Gen Pract. 2022;72(715):70. DOI: 10.3399/bjgp22X718361

URL: https://www.ncbi.nlm.nih.gov/pubmed/35091402
DOI: 10.3399/bjgp22X718361


The occurrence of the omicron variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has importantly impacted surveillance and diagnosis, and has changed the therapeutic landscape of coronavirus disease 2019 (COVID-19). We present the first documented case of locally acquired SARS-CoV-2 omicron variant in Romania in a patient with no recent travel outside the country. We also present the full results of the epidemiological investigation that led to the identification of the index case in a co-worker who had developed mild symptoms shortly after returning from the UK and who had undergone multiple rapid antigen tests with negative results prior to being tested by RT-PCR. We highlight potential lessons learned and describe further directions for actionable research and development in the field of COVID-19.

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The Beijing, 2022 Olympics will be the second Games held amid the COVID-19 pandemic. Due to the unique circumstances the 2022 Games face—the Omicron spread, high virus transmissibility in winters, and uncertainties about vaccine efficacy and future variants of concern, safety measures amid the Beijing 2022 Games will be one of the most intricate among large international events held during the pandemic. To ensure athletes’ health, safety, and ability to participate in the Games, the organizers have introduced the Olympic COVID-free "bubble" protection ecosystem, in which COVID-free athletes could stay and be
protected from potential infections that could upend their Games plans, if not their career as well. However, while staying in the "bubble" is key for athletes' health and success, there is a lack of insights on factors that might prevent athletes from continuing their scheduled Olympic journey as scheduled. To shed light on the issue, based on Beijing, 2022 Olympic Playbooks and most up-to-date guidance issued, this article and its accompanying infographic were developed to illustrate factors that could influence athletes' ability to join and stay in the "bubble", participate in the Games, and further build their career. Furthermore, we also adapted and integrated easy-to-adopt mental health de-stress techniques recommended by the World Health Organization to help athletes better thrive amid the Beijing, 2022 Winter Olympics, in or outside of the "bubble".

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The SARS-CoV-2 pandemic infected 343 million people with over 5.59 million deaths. New mutated lineages of SARS-CoV-2 such as Omicron are evolving faster. Broad-spectrum viral inhibitors that block the initial stage of infection by reducing virus proliferation and disease severity is an unmet global medical need. We studied Bi121, a standardized polyphenolic-rich compound isolated from Pelargonium sidoides, against recombinant Vesicular Stomatitis Virus (rVSV)-pseudotyped SARS-CoV-2 (spike) that represent mutations in the spike protein of six different variants of SARS-CoV-2. Bi121 was effective in neutralizing all six rVSV-Delta-CoV-2S variants expressing different mutations. The antiviral activity of Bi121 was then assessed against three variants of SARS-CoV-2 (USA WA1/2020, Hongkong/VM20001061/2020, B.1.167.2 (Delta)) using RT-qPCR and plaque assays in two different cell lines (Vero cells and HEK-ACE2). Bi121 showed significant activity toward all the three variants tested, suggesting a broad-spectrum activity. Copyright The copyright holder for this preprint is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC 4.0 International license.

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SARS-CoV-2 continues to develop new, increasingly infectious variants including delta and omicron. We evaluated the efficacy of the Abbott BinaxNOW Rapid Antigen Test against Reverse Transcription Polymerase Chain Reaction ("RT-PCR") in 1054 pediatric participants presenting to a high-volume Coronavirus Disease 2019 (COVID-19) testing site while the delta variant was predominant. Participants were grouped by COVID-19 exposure and symptom status. RT-PCR demonstrated an overall prevalence of 5.2%. For all participants, sensitivity of the BinaxNOW was 92.7% (95% CI 82.4%-98.0%) and specificity was 98.0% (95% CI 97.0%-98.8%). For symptomatic participants, positive predictive value (PPV) was 72.7% (95% CI 54.5%-86.7%) and negative predictive value (NPV) was 99.2% (95% CI 98.2%-100%). Among asymptomatic participants, PPV was 71.4% (95% CI 53.7%-85.4%) and NPV was 99.7% (95% CI 99.0%-100%). Our reported sensitivity and NPV are higher than other pediatric studies, potentially because of higher viral load from the delta variant, but specificity and PPV are lower. Importance The BinaxNOW rapid antigen COVID-19 test had a sensitivity of nearly 92% in both symptomatic and asymptomatic children when performed at a high-throughput setting during the more transmissible delta variant dominant period. The test may play an invaluable role in a symptomatic screening and keeping children safe in school. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. All rights reserved. No reuse allowed without permission.

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Background The introduction of the Omicron variant is of significant concern to the Thai Government due to the possibility of a new wave of the COVID-19 epidemic, which may cause a huge strain to the country's health system. This study aims to forecast the trends of COVID-19 cases and deaths given the advent of the Omicron variant in Thailand. Methods We used a compartmental susceptible-exposed-infectious-recovered model in combination with a system dynamics model. We developed four scenarios according to differing values of the production number (R) and varying vaccination rates. Results The findings indicated that in the most pessimistic scenario (R = 7.5 and base vaccination rate), the number of incident cases reached a peak of 49,523 (95% CI: 20,599 to 99,362) by day 73 and the peak daily deaths enlarged to 270 by day 50 (95% CI: 124 to 520). The predicted cumulative cases and deaths at the end of the wave (day 120) were approximately 3.7 million and 22,000 respectively. In the most optimistic assumption (with R = 4.5 and a speedy vaccination rate [tripled the base rate]), the peak of the incident cases was about one third of the most pessimistic assumption (15,650, 95% CI: 12,688 to 17,603). The corresponding daily fatalities were 72 (95% CI: 54 to 84) and the prevalent intubated cases numbered 572 (95% CI: 429 to 675). Conclusions In the coming months, Thailand may face a new wave of the COVID-19 epidemic due to the Omicron variant, the vaccination campaign for the booster dose should be expedited as an effective way of preventing severe illness and death. Copyright The copyright holder for this preprint is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY 4.0 International license.

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DOI: 10.1001/jama.2022.2274


With an increased transmissibility but milder form of disease of the omicron variant of COVID-19 and the newer antivirals often still out of reach of many populations, a refocus of the current treatment regimens is required. Safe, affordable, and available adjuvant treatments should also be considered and known drugs and substances need to be repurposed and tested. Resveratrol, a well-known antioxidant of natural origin, shown to act as an antiviral as well as playing a role in immune stimulation, down regulation of the pro-inflammatory cytokine release and reducing lung injury by reducing oxidative stress, is such an option. New initiatives and collaborations will however need to be found to unleash resveratrol's full potential in the pharmaceutical market.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35240527
DOI: 10.1016/j.biopha.2022.112767

White-tailed deer (Odocoileus virginianus) are highly susceptible to infection by SARS-CoV-2, with multiple reports of widespread spillover of virus from humans to free-living deer. While the recently emerged SARS-CoV-2 B.1.1.529 Omicron variant of concern (VoC) has been shown to be notably more transmissible amongst humans, its ability to cause infection and spillover to non-human animals remains a challenge of concern. We found that 19 of the 131 (14.5%; 95% CI: 0.10-0.22) white-tailed deer opportunistically sampled on Staten Island, New York, between December 12, 2021, and January 31, 2022, were positive for SARS-CoV-2 specific serum antibodies using a surrogate virus neutralization assay, indicating prior exposure. The results also revealed strong evidence of age-dependence in antibody prevalence. A significantly (chi (2), p < 0.001) greater proportion of yearling deer possessed neutralizing antibodies as compared with fawns (OR=12.7; 95% CI4-37.5). Importantly, SARS-CoV-2 nucleic acid was detected in nasal swabs from seven of 68 (10.29%; 95% CI: 0.0-0.20) of the sampled deer, and whole-genome sequencing identified the SARS-CoV-2 Omicron VoC (B.1.1.529) is circulating amongst the white-tailed deer on Staten Island. Phylogenetic analyses revealed the deer Omicron sequences clustered closely with other, recently reported Omicron sequences recovered from infected humans in New York City and elsewhere, consistent with human to deer spillover. Interestingly, one individual deer was positive for viral RNA and had a high level of neutralizing antibodies, suggesting either rapid serological conversion during an ongoing infection or a "breakthrough" infection in a previously exposed animal. Together, our findings show that the SARS-CoV-2 B.1.1.529 Omicron VoC can infect white-tailed deer and highlights an urgent need for comprehensive surveillance of susceptible animal species to identify ecological transmission networks and better assess the potential risks of spillback to humans. Key Findings: These studies provide strong evidence of infection of free-living white-tailed deer with the SARS-CoV-2 B.1.1.529 Omicron variant of concern on Staten Island, New York, and highlight an urgent need for investigations on human-to-animal-to-human spillovers/spillbacks as well as on better defining the expanding host-range of SARS-CoV-2 in non-human animals and the environment.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35169802
DOI: 10.1101/2022.02.04.479189


The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to mutate and evolve with the emergence of omicron (B.1.1.529) as the new variant of concern. The rapid spread of this variant regionally and globally could be an allusion to increased infectivity, transmissibility, and antibody resistance. The omicron variant has a large set of mutations in its spike protein, specifically in the receptor binding domain (RBD), reflecting their significance in ACE2 interaction and antibody recognition. We have carried out the present study to understand how these mutations structurally impact the binding of the antibodies to their target epitope. We have computationally evaluated the binding of different classes of RBD targeted antibodies, namely, CB6 (etesevimab), REGN10933 (casirivimab), S309 (sotrovimab), and S2X259 to the omicron mutation-induced RBD. Molecular dynamics simulations and binding free energy calculations unveil the binding affinity and stability of the antibody-RBD complexes. All the four antibodies show reduced binding affinity towards the omicron RBD. The therapeutic antibody CB6 aka etesevimab was substantially affected due to numerous omicron mutations occurring in its target epitope. This study provides a structural insight into the reduced efficacy of RBD targeting antibodies against the SARS-CoV-2 omicron variant. Copyright The copyright holder for this preprint is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC-ND 4.0 International license.

DOI: 10.1101/2022.01.25.477671

Background: The Omicron SARS-CoV-2 variant is rapidly spreading in the US since December 2021 and is more contagious than earlier variants. Currently, data on the severity of the disease caused by the Omicron variant compared with the Delta variant is limited. Here we compared 3-day risks of emergency department (ED) visit, hospitalization, intensive care unit (ICU) admission, and mechanical ventilation in patients who were first infected during a time period when the Omicron variant was emerging to those in patients who were first infected when the Delta variant was predominant. Method: This is a retrospective cohort study of electronic health record (EHR) data of 577,938 first-time SARS-CoV-2 infected patients from a multicenter, nationwide database in the US during 9/1/2021-12/24/2021, including 14,054 who had their first infection during the 12/15/2021-12/24/2021 period when the Omicron variant emerged ("Emergent Omicron cohort") and 563,884 who had their first infection during the 9/1/2021-12/15/2021 period when the Delta variant was predominant ("Delta cohort"). After propensity-score matching the cohorts, the 3-day risks of four outcomes (ED visit, hospitalization, ICU admission, and mechanical ventilation) were compared. Risk ratios, and 95% confidence intervals (CI) were calculated. Results: Of 14,054 patients in the Emergent Omicron cohort (average age, 36.4 +/- 24.3 years), 27.7% were pediatric patients (<18 years old), 55.4% female, 1.8% Asian, 17.1% Black, 4.8% Hispanic, and 57.3% White. The Emergent Omicron cohort differed significantly from the Delta cohort in demographics, comorbidities, and socio-economic determinants of health. After propensity-score matching for demographics, socioeconomic determinants of health, comorbidities, medications and vaccination status, the 3-day risks in the Emergent Omicron cohort outcomes were consistently less than half those in the Delta cohort: ED visit: 4.55% vs. 15.22% (risk ratio or RR: 0.30, 95% CI: 0.28-0.33); hospitalization: 1.75% vs. 3.95% (RR: 0.44, 95% CI: 0.38-0.52); ICU admission: 0.26% vs. 0.78% (RR: 0.33, 95% CI: 0.23-0.48); mechanical ventilation: 0.07% vs. 0.43% (RR: 0.16, 95% CI: 0.08-0.32). In children under 5 years old, the overall risks of ED visits and hospitalization in the Emergent Omicron cohort were 3.89% and 0.96% respectively, significantly lower than 21.01% and 2.65% in the matched Delta cohort (RR for ED visit: 0.19, 95% CI: 0.14-0.25; RR for hospitalization: 0.36, 95% CI: 0.19-0.68). Similar trends were observed for other pediatric age groups (5-11, 12-17 years), adults (18-64 years) and older adults (>65 years). Conclusions: First time SARS-CoV-2 infections occurring at a time when the Omicron variant was rapidly spreading were associated with significantly less severe outcomes than first-time infections when the Delta variant predominated.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35018384
DOI: 10.1101.2021.12.30.21268495
among all age groups, higher in Black than in White patients (14.0 vs. 3.8), and higher in Hispanic than in non-Hispanic patients (8.9 vs. 3.1). After propensity-score matching for demographics, socio-economic determinants of health, comorbidities and medications, risks for severe clinical outcomes in the Omicron cohort were significantly lower than in the Delta cohort: ED visits: 10.2% vs. 14.6% (risk ratio or RR: 0.70 [0.68-0.71]); hospitalizations: 2.6% vs. 4.4% (RR: 0.58 [0.55-0.60]); ICU admissions: 0.47% vs. 1.00% (RR: 0.47 [0.43-0.51]); mechanical ventilation: 0.08% vs. 0.3% (RR: 0.25 [0.20-0.31]). Similar reduction in disease severity was observed for all age groups. There were significant racial/ethnic and gender disparities in severe clinical outcomes in the Omicron cohort, with Black, Hispanic patients having more ED visits and ICU admissions than White and non-Hispanic patients, respectively, and women had fewer hospitalization and ICU admission than men. Interpretation: The incidence rate of COVID infection during the omicron predominant period (prevalence >92%) was 6-8 times higher than during the Delta predominant period that preceded it consistent with greater infectivity. The incidence rate was highest among those less than 5 years of age, and in Black and Hispanic patients. COVID infections occurring when the Omicron predominated were associated with significantly less frequent severe outcomes than in matched patients when the Delta variant predominated. There were significant racial, ethnic and gender disparities in severe clinical outcomes, with Black and Hispanic patients and men disproportionally impacted.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35233579
DOI: 10.1101/2022.01.12.22269179


Importance: Pediatric SARS-CoV-2 infections and hospitalizations are rising in the US and other countries after the emergence of Omicron variant. However data on disease severity from Omicron compared with Delta in children under 5 in the US is lacking. Objectives: To compare severity of clinic outcomes in children under 5 who contracted COVID infection for the first time before and after the emergence of Omicron in the US. Design Setting and Participants: This is a retrospective cohort study of electronic health record (EHR) data of 79,592 children under 5 who contracted SARS-CoV-2 infection for the first time, including 7,201 infected between 12/26/2021-1/6/2022 when the Omicron predominated (Omicron cohort), 63,203 infected between 9/1/2021-11/15/2021 when the Delta predominated (Delta cohort), and another 9,188 infected between 11/16/2021-11/30/2021 when the Delta predominated but immediately before the Omicron variant was detected in the US (Delta-2 cohort). Exposures: First time infection of SARS-CoV-2. Main Outcomes and Measures: After propensity-score matching, severity of COVID infections including emergency department (ED) visits, hospitalizations, intensive care unit (ICU) admissions, and mechanical ventilation use in the 3-day time-window following SARS-CoV-2 infection were compared between Omicron and Delta cohorts, and between Delta-2 and Delta cohorts. Risk ratios, and 95% confidence intervals (CI) were calculated. Results: Among 7,201 infected children in the Omicron cohort (average age, 1.49 +/- 1.42 years), 47.4% were female, 2.4% Asian, 26.1% Black, 13.7% Hispanic, and 44.0% White. Before propensity score matching, the Omicron cohort were younger than the Delta cohort (average age 1.49 vs 1.73 years), comprised of more Black children, and had fewer comorbidities. After propensity-score matching for demographics, socio-economic determinants of health, comorbidities and medications, risks for severe clinical outcomes in the Omicron cohort were significantly lower than those in the Delta cohort: ED visits: 18.83% vs. 26.67% (risk ratio or RR: 0.71 [0.66-0.75]); hospitalizations: 1.04% vs. 3.14% (RR: 0.33 [0.26-0.43]); ICU admissions: 0.14% vs. 0.43% (RR: 0.32 [0.16-0.66]); mechanical ventilation: 0.33% vs. 1.15% (RR: 0.29 [0.18-0.46]). Control studies comparing Delta-2 to Delta cohorts show no difference. Conclusions and Relevance: For children under age 5, first time SARS-CoV-2 infections occurring when the Omicron predominated (prevalence >92%) was associated with significantly less severe outcomes than first-time infections in similar children when the Delta variant predominated.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35043116
DOI: 10.1101/2022.01.12.22269179
Due to the enormous economic, health, and social costs of the COVID-19 pandemic, there are high expected social returns to investing in parallel in multiple approaches to accelerating vaccination. We argue there are high expected social returns to investigating the scope for lowering the dosage of some COVID-19 vaccines. While existing evidence is not dispositive, available clinical data on the immunogenicity of lower doses combined with evidence of a high correlation between neutralizing antibody response and vaccine efficacy suggests that half or even quarter doses of some vaccines could generate high levels of protection, particularly against severe disease and death, while potentially expanding supply by 450 million to 1.55 billion doses per month, based on supply projections for 2021. An epidemiological model suggests that, even if fractional doses are less effective than standard doses, vaccinating more people faster could substantially reduce total infections and deaths. The costs of further testing alternative doses are much lower than the expected public health and economic benefits. However, commercial incentives to generate evidence on fractional dosing are weak, suggesting that testing may not occur without public investment. Governments could support either experimental or observational evaluations of fractional dosing, for either primary or booster shots. Discussions with researchers and government officials in multiple countries where vaccines are scarce suggest strong interest in these approaches.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35131899
DOI: 10.1073/pnas.2116932119

Changes in the circulation of SARS-CoV-2 variants of concern (VOCs) may require changes in public health response to the COVID-19 pandemic, as they have the potential to evade vaccines and pharmaceutical interventions and may be more transmissible relative to other SARS-CoV-2 variants. As such, it is essential to track and prevent their spread in susceptible communities. We developed digital RT-PCR assays for mutations characteristic of VOCs and used them to quantify those mutations in wastewater settled solids samples collected from a publicly owned treatment works (POTW) during different phases of the COVID-19 pandemic. Wastewater concentrations of single mutations characteristic to each VOC, normalized by the concentration of a conserved SARS-CoV-2 N gene, correlate to regional estimates of the proportion of clinical infections caused by each VOC. These results suggest targeted RT-PCR assays can be used to detect variants circulating in communities and inform public health response to the pandemic. Importance (150 words) Wastewater represents a pooled biological sample of the contributing community and thus a resource of assessing community health. Here we show that emergence, spread, and disappearance of SARS-CoV-2 infections caused by variants of concern are reflected in the presence of variant genomic RNA in wastewater settled solids. This work highlights an important public health use case for wastewater. Copyright The copyright holder for this preprint is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-ND 4.0 International license.

DOI: 10.1101/2022.01.17.22269439

Recently emerged variants of SARS-CoV-2 contain in their surface spike glycoproteins multiple substitutions associated with increased transmission and resistance to neutralising antibodies. We have examined the structure and receptor binding properties of spike proteins from the B.1.1.7 (Alpha) and B.1.351 (Beta) variants to better understand the evolution of the virus in humans. Spikes of both variants have the same mutation, N501Y, in the receptor-binding domains. This substitution confers tighter ACE2 binding, dependent on the common earlier substitution, D614G. Each variant’s spike has acquired other key changes in structure that likely impact virus pathogenesis. The spike from the Alpha variant is more stable against
disruption upon binding ACE2 receptor than all other spikes studied. This feature is linked to the
acquisition of a more basic substitution at the S1-S2 furin site (also observed for the variants of concern
Delta, Kappa, and Omicron) which allows for near-complete cleavage. In the Beta variant spike, the
presence of a new substitution, K417N (also observed in the Omicron variant), in combination with the
D614G, stabilises a more open spike trimer, a conformation required for receptor binding. Our
observations suggest ways these viruses have evolved to achieve greater transmissibility in humans.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35246509
DOI: 10.1038/s41467-022-28768-w

152. Yadav PD, Sapkal GN, Sahay RR, et al. Substantial immune response in Omicron infected breakthrough
and unvaccinated individuals against SARS-CoV-2 variants of concerns. bioRxiv. 2022. DOI:
10.1101/2022.01.24.477043
The recent emergence of highly mutated SARS-CoV-2 Omicron variant has debilitating effect on public health
system of the affected countries worldwide. Currently India is facing third wave of COVID-19 pandemic
and going through a severe crisis. Within short span of time, the variant has shown high transmissibility
and capability of evading the immune response generated against natural infection and vaccination. The
immune escape potential of Omicron is a serious concern and further needs to be explored. In the present
study, we have assessed the IgG and neutralizing antibody (NAb) response in breakthrough individuals
vaccinated with two doses ChAdOx1 nCoV-19 vaccine (n=25), breakthrough individuals vaccinated with
two doses of BNT162b2 mRNA vaccine (n=8) and unvaccinated individuals (n=6). All these individuals
were infected with Omicron variant. The IgG antibody activity in the sera of the ChAdOx1 nCoV-19 and
BNT162b2 mRNA breakthrough individuals was comparable with S1-RBD, while it was lesser in BNT162b2
mRNA breakthrough individuals with N protein and inactivated whole antigen IgG ELISA. BNT162b2 mRNA
breakthrough individuals showed moderate reduction in NAb GMTs compared to ChAdOx1 nCoV-19
against Alpha, Beta and Delta. However, 3-fold higher reduction was observed with omicron variant in
BNT162b2 mRNA than ChAdOx1 nCoV-19. Apparently, Alpha variant was modestly resistant to the sera of
unvaccinated individuals than Beta, Delta and Omicron. Our study demonstrated substantial immune
response in the individuals infected with Omicron. The neutralizing antibodies could effectively neutralize
the Omicron and other VOCs including the most prevalent Delta variant. Copyright The copyright holder
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DOI: 10.1101/2022.01.24.477043

persistence of anti-SARS-CoV-2 humoral and cellular immunity. Emerg Microbes Infect. 2022:1-43. DOI:
10.1080/22221751.2022.2049984
The immune memory of over 400 million COVID-19 convalescents is not completely understood. In this integrated
study, we recorded the post-acute sequelae symptoms and tested the immune memories, including
circulating antibodies, memory B cell, and memory CD4 or CD8 T cell responses of a cohort of 65 COVID-
19 patients over 1-year after infection. Our data show that 48% of them still have one or more sequelae
symptoms and all of them maintain at least one of the immune components. The chances of having
sequelae symptoms or having better immune memory are associated with peak disease severity. We did
time points sampling per subject to precisely understand the kinetics of durability of SARS-CoV-2
circulating antibodies. We found that the RBD IgG levels likely reach a stable plateau at around 6 months,
although it is waning at the first 6 months after infection. At 1-year after infection, more than 90% of the
convalescents generated memory CD4 or CD8 T memory responses, preferably against the SARS-CoV-2 M
peptide pool. The convalescents also have polyfunctional and central memory T cells that could provide
rapid and efficient response to SARS-CoV-2 re-infection. Based on this information, we assessed the
immune protection against the Omicron variant and concluded that convalescents should still induce
effective T cell immunity against the Omicron. By studying the circulating antibodies and memory B or T
cell responses to SARS-CoV-2 in an integrated manner, our study provides insight into the understanding of protective immunity against diseases caused by secondary SARS-CoV-2 infection.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35240947
DOI: 10.1080/22221751.2022.2049984


The newly emerging SARS-CoV-2 Omicron (B.1.1.529) variant first identified in South Africa in November 2021 is characterized by an unusual number of amino acid mutations in its spike that renders existing vaccines and therapeutic monoclonal antibodies dramatically less effective. The in vivo pathogenicity, transmissibility, and fitness of this new Variant of Concern are unknown. We investigated these virological attributes of the Omicron variant in comparison with those of the currently dominant Delta (B.1.617.2) variant in the golden Syrian hamster COVID-19 model. Omicron-infected hamsters developed significantly less body weight losses, clinical scores, respiratory tract viral burdens, cytokine/chemokine dysregulation, and tissue damages than Delta-infected hamsters. The Omicron and Delta variant were both highly transmissible (100% vs 100%) via contact transmission. Importantly, the Omicron variant consistently demonstrated a about 10-20% higher transmissibility than the already-highly transmissible Delta variant in repeated non-contact transmission studies (overall: 30/36 vs 24/36, 83.3% vs 66.7%). The Delta variant displayed higher fitness advantage than the Omicron variant without selection pressure in both in vitro and in vivo competition models. However, this scenario drastically changed once immune selection pressure with neutralizing antibodies active against the Delta variant but poorly active against the Omicron variant were introduced, with the Omicron variant significantly outcompeting the Delta variant. Taken together, our findings demonstrated that while the Omicron variant is less pathogenic than the Delta variant, it is highly transmissible and can outcompete the Delta variant under immune selection pressure. Next-generation vaccines and antivirals effective against this new VOC are urgently needed. Copyright The copyright holder for this preprint is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under a CC-BY-NC-ND 4.0 International license.

DOI: 10.1101/2022.01.12.476031


URL: https://www.ncbi.nlm.nih.gov/pubmed/35041829
DOI: 10.1016/j.jamda.2021.12.035


With the increased prevalence of new SARS-CoV-2 variants of concern, such as Delta and Omicron, the COVID-19 pandemic has become an ongoing human health disaster, killing millions worldwide. SARS-CoV-2 invades its host through the interaction of its spike (S) protein with a host cell receptor, angiotensin-converting enzyme 2 (ACE2). In addition, heparan sulfate (HS) on the surface of host cells plays an important role as a co-receptor for this viral pathogen-host cell interaction. Our previous studies demonstrated that many sulfated glycans, such as heparin, fucoidans, and rhamnan sulfate have anti-SARS-CoV-2 activities. In the current study, a small library of sulfated glycans and highly negatively charged compounds, including pentosan polysulfate (PPS), mucopolysaccharide polysulfate (MPS), sulfated lactobionic acid, sulodexide, and defibrotide, was assembled and evaluated for binding to the S-proteins and inhibition of viral infectivity in vitro. These compounds inhibited the interaction of the S-protein receptor-binding domain (RBD) (wild type and different variants) with immobilized heparin, a highly sulfated HS, as determined using surface plasmon resonance (SPR). PPS and MPS showed the strongest inhibition of interaction of...
heparin and S-protein RBD. The competitive binding studies showed that the IC50 of PPS and MPS against the S-protein RBD binding to immobilized heparin was ~35 nM and ~9 nM, respectively, much lower than the IC50 for soluble heparin (IC50 = 56 nM). Both PPS and MPS showed stronger inhibition than heparin on the S-protein RBD or spike pseudotyped lentiviral particles binding to immobilized heparin. Finally, in an in vitro cell-based assay, PPS and MPS exhibited strong antiviral activities against pseudotyped viral particles of SARS-CoV-2 containing wild-type or Delta S-proteins.

URL: https://www.ncbi.nlm.nih.gov/pubmed/35215371
DOI: 10.3390/ph15020258

URL: https://www.ncbi.nlm.nih.gov/pubmed/34914506
DOI: 10.1126/science.acz9834

URL: https://www.ncbi.nlm.nih.gov/pubmed/34882443
DOI: 10.1126/science.acx9782


OBJECTIVE: The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has created a challenging and threatening situation worldwide. The SARS-CoV-2 embodies diverse epidemiological trends, alongside emerging and reemerging pathogenic characteristics, which have raised great public health concerns. This study aims to investigate the global prevalence, biological and clinical characteristics of Omicron, a new variant of SARS-CoV-2 that is causing concern and fear internationally. MATERIALS AND METHODS: The data on the outbreak of the new variant "Omicron" was obtained from the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC), European Centre for Disease Prevention and Control (ECDC), research institutes, and global international print media. We recorded information on the prevalence, the biological and clinical characteristics of the Omicron Variant of SARS-CoV-2 from November 24 to December 9, 2021. RESULTS: Worldwide, the new variant of SARS-CoV-2, Omicron, has been identified in 57 countries with 2152 confirmed cases reported on December 9, 2021, ever since the emergence of the first case of this variant dated November 24, 2021. The number of confirmed Omicron variant cases has significantly increased globally. The novel variant is spreading swiftly and has crossed many borders all around the world. This new variant has been observed to be transmitted far more rapidly than other variants of SARS-CoV-2. CONCLUSIONS: The new variant of SARS-CoV-2 has novel epidemiological and biological characteristics, making it more contagious than other variants of SARS-CoV-2. It has affected 2152 people in 57 countries in a short period of two weeks. However, the fatality rate of the SARS-CoV-2 Omicron variant has not yet been reported. The major clinical manifestations in this new variant are those of a "mild infection", including headache, body ache, muscles ache, cough, fever, generalized myalgia, and severe fatigue. It is infecting younger and middle-aged people more than previous variants. Worldwide health establishments should take immediate preventive measures to stop outbreaks of this emerging and reemerging pathogenic variant across the globe to minimize the disease burden on humanity.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34982465
DOI: 10.26355/eurrev_202112_27652
The SARS-CoV2 Omicron variant has sparked global concern due to the possibility of enhanced transmissibility and escape from vaccines and therapeutics. In this study, we describe the mutational landscape of the Omicron variant using amino acid interaction (AAI) networks. AAI network analysis is particularly well suited for interrogating the impact of constellations of mutations as occur on Omicron that may function in an epistatic manner. Our analyses suggest that as compared to previous variants of concern, the Omicron variant has increased antibody escape breadth due to mutations in class 3 and 4 antibody epitopes as well as increased escape depth due to accumulated mutations in class 1 antibody epitopes. We note certain RBD mutations that might further enhance Omicron's escape, and in particular advise careful surveillance of two subclades bearing R346S/K mutations with relevance for certain therapeutic antibodies. Further, AAI network analysis suggests that the function of certain therapeutic monoclonal antibodies may be disrupted by Omicron mutations as a result of the cumulative indirect perturbations to the epitope surface properties, despite point-mutation analyses suggesting these antibodies are tolerant of the set of Omicron mutations in isolation. Finally, for several Omicron mutations that do not appear to contribute meaningfully to antibody escape, we find evidence for a plausible role in enhanced transmissibility via disruption of RBD-down conformational stability at the RBD-RBD interface.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34909771
DOI: 10.1101/2021.12.06.471499

There is a growing concern that ongoing evolution of SARS-CoV-2 could lead to variants of concern (VOC) that are capable of avoiding some or all of the multi-faceted immune response generated by both prior infection or vaccination, with the recently described B.1.1.529 (Omicron) VOC being of particular interest. Peripheral blood mononuclear cell samples from PCR-confirmed, recovered COVID-19 convalescent patients (n=30) infected with SARS-CoV-2 in the United States collected in April and May 2020 who possessed at least one or more of six different HLA haplotypes were selected for examination of their anti-SARS-CoV-2 CD8+ T-cell responses using a multiplexed peptide-MHC tetramer staining approach. This analysis examined if the previously identified viral epitopes targeted by CD8+ T-cells in these individuals (n=52 distinct epitopes) are mutated in the newly described Omicron VOC (n=50 mutations). Within this population, only one low-prevalence epitope from the Spike protein restricted to two HLA alleles and found in 2/30 (7%) individuals contained a single amino acid change associated with the Omicron VOC. These data suggest that virtually all individuals with existing anti-SARS-CoV-2 CD8+ T-cell responses should recognize the Omicron VOC, and that SARS-CoV-2 has not evolved extensive T-cell escape mutations at this time. Importance: The newly identified Omicron variant of concern contains more mutations than any of the previous variants described to date. In addition, many of the mutations associated with the Omicron variant are found in areas that are likely bound by neutralizing antibodies, suggesting that the first line of immunological defense against COVID-19 may be compromised. However, both natural infection and vaccination develop T-cell based responses, in addition to antibodies. This study examined if the parts of the virus, or epitopes, targeted by the CD8+ T-cell response in thirty individuals who recovered from COVID-19 in 2020 were mutated in the Omicron variant. Only one of 52 epitopes identified in this population contained an amino acid that was mutated in Omicron. These data suggest that the T-cell immune response in previously infected, and most likely vaccinated individuals, should still be effective against Omicron.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34909772
DOI: 10.1101/2021.12.06.471446

Appendix 1: Evidence Search Details
Filters, Limits & Exclusions: English only [March 04, 2022 – March 11, 2022] …

Sources Searched:
- Alberta Health Services
- BCCDC
- CDC
- CINAHL
- City of Toronto
- Cochrane
- COVID-End
- ECDC
- Embase (Ovid)
- Evidence Check Australia
- FDA
- Google
- Google Scholar
- Government of Ireland
- Health Canada/PHAC
- Health Information and Quality Authority
- HSE Ireland
- Imperial College London

Librarian(s):
- Mark Mueller, Clinical Librarian, Saskatchewan Health Authority
- Lukas Miller, Clinical Librarian, Saskatchewan Health Authority

Appendix 2: Search Strategies

Keywords Used in Other Resources
- "B.1.1.529" or "B11529" or "GR/484A" or "BA.2" or omicron

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