Saskatchewan Health Authority

University of Saskatchewan

COVID-19 Evidence Support Team
EVIDENCE SEARCH REPORT

Review Question:	What is the epidemiology of variants and what are the implications for healthcare?
Context:	Update for ongoing review
Review Code:	EOC031801v020 ESR **Complete Date:** December 17, 2021
Cite As:	Miller, L., Howell-Spooner, B.. What is the epidemiology of variants and what are the implications for healthcare? 2021 Dec 17, Document no.: EOC031801v020 ESR. In: COVID-19 Rapid Evidence Reviews [Internet]. SK: SK COVID Evidence Support Team, c2021. 43 p. (CEST evidence search report).

Librarian Notes & Comments

Hello All,
Here is the update on the COVID-19 variants from December 3, 2021, to December 17, 2021.

Sincerely,
Lukas and Brianna

Search Results: Guidelines, Summaries & Other Grey Literature

Government

Public Health England / UK Health Security Agency / UK Parliament

- SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 31. 10 December 2021. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1040076/Technical_Briefing_31.pdf
- SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 31. 3 December 2021. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1038404/Technical_Briefing_30.pdf
- Research Briefing: Omicron and new coronavirus variants. 10 December 2021. https://commonslibrary.parliament.uk/research-briefings/cbp-9400/

Government of Canada

Disclaimer

- Federal Ministers will make announcements regarding new measures to address the Omicron variant of concern. 15 December 2021. CDChttps://www.canada.ca/en/public-health/news/2021/12/federal-ministers-will-make-announcements-regarding-new-measures-to-address-the-omicron-variant-of-concern.html

Public Health Ontario

- Evidence Brief: Variant of Concern Omicron (B.1.1.529): Risk Assessment, December 7, 2021. https://www.publichealthontario.ca/-/media/documents/ncov/voc/2021/12/covid-19-omicron-b11529-risk-assessment-dec-7.pdf?sc_lang=en
- Enhanced Epidemiological Summary – Early Dynamics of Omicron in Ontario, November 1 to December 9, 2021. 14 December 2021. https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-early-dynamics-omicron-ontario-epi-summary.pdf?sc_lang=en

Alberta Health Services

- Laboratory Bulletin: SARS-CoV-2 Variant of Concern Update 10 December 2021. https://www.albertahealthservices.ca/assets/wf/lab/if-lab-hp-bulletin-sars-cov-2-variant-of-concern-update.pdf

Centers for Disease Control and Prevention

- What You Need to Know About Variants. 13 December 2021. https://www.cdc.gov/coronavirus/2019-ncov/variants/about-variants.html https://www.cdc.gov/coronavirus/2019-ncov/variants/omicron-variant.html
- MMWR: SARS-CoV-2 B.1.1.529 (Omicron) Variant — United States, December 1–8, 2021. 17 December 2021. https://www.cdc.gov/mmwr/volumes/70/wr/mm7050e1.htm
    - Cited in reference list below, as well.

City of Toronto

- City of Toronto fully reactivates Emergency Operations Centre in response to Omicron variant of concern. 17 December 2021. https://www.toronto.ca/news/city-of-toronto-fully-reactivates-emergency-operations-centre-in-response-to-omicron-variant-of-concern/

Agencies

ECDC

- SARS-CoV-2 variants of concern as of 16 December 2021 https://www.ecdc.europa.eu/en/covid-19/variants-concern
- ECDC publishes new risk assessment on further emergence of Omicron variant https://www.ecdc.europa.eu/en/news-events/ecdc-publishes-new-risk-assessment-further-emergence-omicron-variant
- Epidemiological update: Omicron variant of concern (VOC) – data as of 16 December 2021 (12:00) https://www.ecdc.europa.eu/en/news-events/epidemiological-update-omicron-data-16-december
- Epidemiological update: Omicron variant of concern (VOC) – data as of 15 December 2021 (12:00) https://www.ecdc.europa.eu/en/news-events/epidemiological-update-omicron-data-15-december

- Epidemiological update: Omicron variant of concern (VOC) – data as of 14 December 2021 (12:00) https://www.ecdc.europa.eu/en/news-events/epidemiological-update-omicron-variant-concern-voc-data-14-december-2021
- Epidemiological update: Omicron variant of concern (VOC) – data as of 13 December 2021 (12:00) https://www.ecdc.europa.eu/en/news-events/epidemiological-update-omicron-data-13-december
- Epidemiological update: Omicron variant of concern (VOC) – data as of 12 December 2021 (12:00) https://www.ecdc.europa.eu/en/news-events/epidemiological-update-omicron-data-12-december
- Additional prior updates available via https://www.ecdc.europa.eu/en/news-events

WHO / PAHO

- Omicron and other variants of concern identified in the Americas. December 3, 2021. https://www.paho.org/en/news/3-12-2021-omicron-and-other-variants-concern-identified-americas
- What you need to know about the new Omicron COVID-19 variant December 3 2021. https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/news/2021/12/what-you-need-to-know-about-the-new-omicron-covid-19-variant
- Variant of Concern (VOC) Delta to Omicron, Transmissibility, Severity, Impact of Social Mobility - What will drive future trends and Optimizing our response https://www.paho.org/en/news/16-12-2021-variant-concern-voc-delta-omicron-transmissibility-severity-impact-social-mobility
- Enhancing Readiness for Omicron (B.1.1.529): Technical Brief and Priority Actions for Member States. 10 December 2021. https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states

Research Centres

National Collaborating Centre for Infectious Disease

- Updates on COVID-19 Variants of Concern. 10 December 2021. https://nccid.ca/covid-19-variants/

Imperial College London

- Report 49 - Growth, population distribution and immune escape of Omicron in England. 16 December 2021. https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-49-omicron/
- Report 48 - The value of vaccine booster doses to mitigate the global impact of the Omicron SARS-CoV-2 variant. 16 December 2021. https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-48-global-omicron/
- Omicron - latest findings and commentary from Imperial experts. 10 December 2021 https://www.imperial.ac.uk/news/232614/omicron-latest-findings-commentary-from-imperial/

COVID-NMA (Network Meta-Analysis)

- COVID-19 Vaccine Effectiveness on Variants of Concern: Randomized Evidence. [updates bi-weekly. Last update December 17) https://covid-nma.com/vaccines/variants/
- COVID-19 Vaccine Effectiveness on Variants of Concern: Observational Studies [updated biweekly. Last update December 17] https://covid-nma.com/vaccines/os_vaccines/
    - Includes appraised table of evidence and forest plots.

Search Results: News, Blogs, & Social Media

News

CBC

- Why omicron is overtaking delta — and what that means for our fight against COVID-19. 13 December 2021. https://www.cbc.ca/news/health/why-omicron-is-overtaking-delta-and-what-that-means-for-our-fight-against-covid-19-1.6283611
- Experts warn Sask. residents, government to take measures as Omicron variant spreads. 16 December 2021 https://www.cbc.ca/news/canada/saskatchewan/experts-warn-sask-residents-government-to-take-precautionary-measures-against-new-omicron-variant-1.6285226

CTV News

- Four numbers that outline why Omicron is causing so much concern. 15 December 2021. https://www.ctvnews.ca/health/coronavirus/four-numbers-that-outline-why-omicron-is-causing-so-much-concern-1.5709252
- Ontario needs to address myth that Omicron is mild, head of science table says. 13 December 2021. https://toronto.ctvnews.ca/ontario-needs-to-address-myth-that-omicron-is-mild-head-of-science-table-says-1.5705025
- Omicron spread may overwhelm hospitals once again, experts warn. 14 December 2021. https://www.ctvnews.ca/health/coronavirus/omicron-spread-may-overwhelm-hospitals-once-again-experts-warn-1.5706461

Global News

- Omicron COVID-19 variant outlook for Canada has feds 'very concerned,' Trudeau says. 13 December 2021. https://globalnews.ca/news/8446281/omicron-covid-variant-cases-canada-trudeau/

CIDRAP

- Uncertainty swirls around Omicron COVID-19 severity. 17 December 2021. https://www.cidrap.umn.edu/news-perspective/2021/12/uncertainty-swirls-around-omicron-covid-19-severity
- Omicron boosts COVID-19 surges in Denmark, UK. 16 December 2021. https://www.cidrap.umn.edu/news-perspective/2021/12/omicron-boosts-covid-19-surges-denmark-uk
- COVID-19 Scan for Dec 16, 2021. https://www.cidrap.umn.edu/news-perspective/2021/12/covid-19-scan-dec-16-2021
- US hits 800,000 COVID-19 deaths as Omicron now in 36 states. 15 December 2021. https://www.cidrap.umn.edu/news-perspective/2021/12/us-hits-800000-covid-19-deaths-omicron-now-36-states

American Society for Microbiology

- How Ominous Is the Omicron Variant (B.1.1.529)? 16 December 2021. https://asm.org/Articles/2021/December/How-Ominous-is-the-Omicron-Variant-B-1-1-529

Science.org

- How bad is Omicron? Some clues are emerging, and they're not encouraging. December 7, 2021. https://www.science.org/content/article/how-bad-omicron-some-clues-are-emerging-and-they-re-not-encouraging

Search Results: Journal Articles (includes preprints)

Sorted by newest-oldest.

1. Stampfer SD, Goldwater MS, Bujarski S, et al. Severe breakthrough COVID-19 with a heavily mutated variant in a multiple myeloma patient 10 weeks after vaccination. Clin Infect Pract. 2022;13:100130. DOI: 10.1016/j.clinpr.2021.100130
ABSTRACT: Background: Patients with multiple myeloma have unpredictable responses to vaccination for COVID-19. Anti-spike antibody levels can determine which patients develop antibodies at levels similar to healthy controls, and are a known correlate of protection. Case report: A multiple myeloma patient developed protective anti-spike antibodies after vaccination (608 IU/mL), but nonetheless developed severe breakthrough COVID-19 just 10 weeks following his second vaccination with mRNA-1273. Results: Sequencing of the viral isolate revealed an extensively mutated variant with 10 spike protein mutations, including E484Q and N440K. Serology testing showed a dramatic decline in anti-spike antibodies immediately prior to virus exposure. Conclusions: Multiple myeloma patients who do develop detectable antibody responses to vaccination may be at increased risk for breakthrough infections due to rapid decline in antibody levels. Viral variants with immune escape mutations such as N440K, also seen independently in the SARS-CoV-2 Omicron variant (B.1.1.529) and in viral passaging experiments, likely require a higher level of anti-spike antibodies to prevent severe COVID-19.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34909634
DOI: 10.1016/j.clinpr.2021.100130

2. Swamy S, Koch CA, Hannah-Shmouni F, et al. Hypertension and COVID-19: Updates from the era of vaccines and variants. J Clin Transl Endocrinol. 2022;27:100285. DOI: 10.1016/j.jcte.2021.100285
ABSTRACT: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathogen responsible for coronavirus disease 2019 (COVID-19) has been a major cause of morbidity and mortality globally. Older age, and the presence of certain components of metabolic syndrome, including hypertension have been associated with increased risk for severe disease and death in COVID-19 patients. The role of antihypertensive agents in the pathogenesis of COVID-19 has been extensively studied since the onset of the pandemic. This review discusses the potential pathophysiologic interactions between hypertension and COVID-19 and provides an up-to-date information on the implications of newly emerging SARS-CoV-2 variants, and vaccines on patients with hypertension.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34900602
DOI: 10.1016/j.jcte.2021.100285

3. Abbasi J. Omicron Has Reached the US-Here's What Infectious Disease Experts Know About the Variant. JAMA. 2021;06:06-. DOI: 10.1001/jama.2021.22619
URL: https://www.ncbi.nlm.nih.gov/pubmed/34870691
DOI: 10.1001/jama.2021.22619

4. Aggarwal A, Ospina Stella A, Walker G, et al. SARS-CoV-2 Omicron: reduction of potent humoral responses and resistance to clinical immunotherapeutics relative to viral variants of concern. medRxiv. 2021:2021.12.14.21267772. DOI: 10.1101/2021.12.14.21267772
ABSTRACT: From late 2020 the world observed the rapid emergence of many distinct SARS-CoV-2 variants. At the same time, pandemic responses resulted in significant global vaccine rollouts that have now significantly lowered Covid-19 hospitalisation and mortality rates in the developed world. Unfortunately, in late 2021, the variant Omicron (B.1.1.529) emerged and it eclipsed the other variants of concern (VOC) in its number of Spike polymorphisms, and its ability to compete with and displacement of the dominant VOC Delta. Herein we accessed the impact of Omicron to humoral neutralisation in vaccinated, convalescent cohorts, in concentrated human IgG

from thousands of plasma donors and also alongside many clinically used monoclonal antibodies. Overall, we observed a 17 to 22 fold drop in neutralisation titres across all donors that reached a titre to Omicron. Concentrated pooled human IgG from convalescent and vaccinated donors had greater breadth but was still reduced by 16-fold. In all therapeutic antibodies tested, significant neutralization was only observed for Sotrovimab, with other monoclonals unable to neutralize B.1.1.529.Competing Interest StatementThe authors have declared no competing interest.Funding StatementThis work was supported by The University of New South Wales Rapid Response grant (Australia, ADK), the Medical Research Future Fund COVID-19 grant (MRFF2005760, SGT), Medical Research Future Fund Antiviral Development Call grant (DC), Medical Research Future Fund COVID-19 grant (MRFF2001684, ADK), the New South Wales Health COVID-19 Research Grants Round 2 (FB). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.Author DeclarationsI confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained.YesThe details of the IRB/oversight body that provided approval or exemption for the research described are given below: All human serum samples were obtained with written informed consent from the participants under ethics approvals of St Vincent's Hospital Ethics Committee 2020/ETH00964 and Westmead Hospital Ethics Committee 2020/ETH02068).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.YesI 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.YesAll data produced in the present work are contained in the manuscript
URL: http://medrxiv.org/content/early/2021/12/15/2021.12.14.21267772.abstract
DOI: 10.1101/2021.12.14.21267772

5. Alexander W, Marek W, Katharina G, et al. Reduced Neutralization of SARS-CoV-2 Omicron Variant by Vaccine Sera and monoclonal antibodies. 2021.
ABSTRACT: Due to numerous mutations in the spike protein, the SARS-CoV-2 variant of concern Omicron (B.1.1.529) raises serious concerns since it may significantly limit the antibody-mediated neutralization and increase the risk of reinfections. While a rapid increase in the number of cases is being reported worldwide, until now there has been uncertainty about the efficacy of vaccinations and monoclonal antibodies. Our in vitro findings using authentic SARS-CoV-2 variants indicate that in contrast to the currently circulating Delta variant, the neutralization efficacy of vaccine-elicited sera against Omicron was severely reduced highlighting T-cell mediated immunity as essential barrier to prevent severe COVID-19. Since SARS-CoV-2 Omicron was resistant to casirivimab and imdevimab, genotyping of SARS-CoV-2 may be needed before initiating mAb treatment. Variant-specific vaccines and mAb agents may be required to treat COVID-19 due to Omicron and other emerging variants of concern.
URL: https://medrxiv.org/cgi/content/short/2021.12.07.21267432

6. Anonymous. Omicron is bad but the global response is worse. Nature. 2021;600(7888):190. DOI: 10.1038/d41586-021-03616-x
URL: https://www.ncbi.nlm.nih.gov/pubmed/34876667
DOI: 10.1038/d41586-021-03616-x

7. Babiker A, Immergluck K, Stampfer SD, et al. Single-Amplicon Multiplex Real-Time Reverse Transcription-PCR with Tiled Probes To Detect SARS-CoV-2 spike Mutations Associated with Variants of Concern. J Clin Microbiol. 2021;59(12):e0144621. DOI: 10.1128/JCM.01446-21
ABSTRACT: To provide an accessible and inexpensive method to surveil for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mutations, we developed a multiplex real-time reverse transcription-PCR (rRT-PCR) assay, the Spike single-nucleotide polymorphism (SNP) assay, to detect specific mutations in the spike receptor

binding domain. A single primer pair was designed to amplify a 348-bp region of spike, and probes were initially designed to detect K417, E484K, and N501Y. The assay was evaluated using characterized variant sample pools and residual nasopharyngeal samples. Variant calls were confirmed by SARS-CoV-2 genome sequencing in a subset of samples. Subsequently, a fourth probe was designed to detect L452R. The lower limit of 95% detection was 2.46 to 2.48 log10 genome equivalents (GE)/ml for the three initial targets (approximately 1 to 2 GE/reaction). Among 253 residual nasopharyngeal swabs with detectable SARS-CoV-2 RNA, the Spike SNP assay was positive in 238 (94.1%) samples. All 220 samples with threshold cycle (CT) values of <30 for the SARS-CoV-2 N2 target were detected, whereas 18/33 samples with N2 CT values of >/=30 were detected. Spike SNP results were confirmed by sequencing in 50/50 samples (100%). Addition of the 452R probe did not affect performance for the original targets. The Spike SNP assay accurately identifies SARS-CoV-2 mutations in the receptor binding domain, and it can be quickly modified to detect new mutations that emerge.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34432488
DOI: 10.1128/JCM.01446-21

8. Barnard RC, Davies NG, Pearson CAB, et al. Projected epidemiological consequences of the Omicron SARS-CoV-2 variant in England, December 2021 to April 2022. medRxiv. 2021:2021.12.15.21267858. DOI: 10.1101/2021.12.15.21267858
ABSTRACT: The Omicron B.1.1.529 SARS-CoV-2 variant was first detected in late November 2021 and has since spread to multiple countries worldwide. We model the potential consequences of the Omicron variant on SARS-CoV-2 transmission and health outcomes in England between December 2021 and April 2022, using a deterministic compartmental model fitted to epidemiological data from March 2020 onwards. Because of uncertainty around the characteristics of Omicron, we explore scenarios varying the extent of Omicron's immune escape and the effectiveness of COVID-19 booster vaccinations against Omicron, assuming the level of Omicron's transmissibility relative to Delta to match the growth in observed S gene target failure data in England. We consider strategies for the re-introduction of control measures in response to projected surges in transmission, as well as scenarios varying the uptake and speed of COVID-19 booster vaccinations and the rate of Omicron's introduction into the population. These results suggest that Omicron has the potential to cause substantial surges in cases, hospital admissions and deaths in populations with high levels of immunity, including England. The reintroduction of additional non-pharmaceutical interventions may be required to prevent hospital admissions exceeding the levels seen in England during the previous peak in winter 2020-2021.Competing Interest StatementRCB, NGD, MJ and WJE are participants of the UK's Scientific Pandemic Influenza Group on Modelling (SPI-M). WJE attends the UK's Scientific Advisory Group for Emergencies. All authors declare no competing interests.Funding StatementThe following funding sources are acknowledged as providing funding for the named authors. This project has received funding from the European Union's Horizon 2020 research and innovation programme - project EpiPose (101003688: RCB, MJ, WJE) and the UK Medical Research Council (MC_PC_19065: NGD, WJE). It was also partly funded by the Bill & Melinda Gates Foundation (INV-003174 and INV-016832: MJ) and the National Institute for Health Research (NIHR) (Health Protection Research Unit for Immunisation NIHR200929: NGD, MJ; Health Protection Research Unit in Modelling and Health Economics NIHR200908: MJ, WJE; PR-OD-1017-20002: WJE). CABP is supported by the Bill & Melinda Gates Foundation (OPP1184344) and the UK Foreign, Commonwealth and Development Office (FCDO)/Wellcome Trust Epidemic Preparedness Coronavirus research programme (ref. 221303/Z/20/Z).Author DeclarationsI confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained.YesThe details of the IRB/oversight body that provided approval or exemption for the research described are given below:Ethical approval for this research was given by the London School of Hygiene & Tropical Medicine Ethics Committee, project ID: 22828.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.YesI 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.YesData sources used for these analyses are either publicly available, or were provided to RCB and NGD as members of the UK& 039;s Scientific Pandemic Influenza Modelling (SPI-M) group, which provides expert advice to the UK's Department of Health and Social Care and wider UK government on scientific matters. Specific permissions have been sought to use SPI-M data for this publication. The SPI-M datasets used for model fitting are unpublished and not publicly available, but are closely aligned with the UK Government's COVID-19 dashboard (see https://coronavirus.data.gov.uk/) and other publicly available sources such as the Wellcome Sanger Institute's COVID-19 genomic surveillance data (see https://covid19.sanger.ac.uk/downloads).
URL: http://medrxiv.org/content/early/2021/12/16/2021.12.15.21267858.abstract
DOI: 10.1101/2021.12.15.21267858

9. Bartha FA, Boldog P, Dénes A, et al. Potential severity, mitigation, and control of Omicron waves depending on pre-existing immunity and immune evasion. medRxiv. 2021:2021.12.15.21267884. DOI: 10.1101/2021.12.15.21267884
ABSTRACT: We assess the potential consequences of the upcoming SARS-CoV-2 waves caused by the Omicron variant. Our results suggest that even in those regions where the Delta variant is controlled at the moment by a combination of non-pharmaceutical interventions and population immunity, a significant Omicron wave can be expected. We stratify the population according to prior immunity status, and characterize the possible outbreaks depending on the population level of pre-existing immunity and the immune evasion capability of Omicron. We point out that two countries having similar effective reproduction numbers for the Delta variant can experience very different Omicron waves in terms of peak time, peak size and total number of infections among the high risk population.Competing Interest StatementThe authors have declared no competing interest.Funding StatementHungarian National Research, Development, and Innovation Office (NKFIH)Author DeclarationsI confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained.YesI 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.YesI 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.YesThe present study did not produce any new data.
URL: http://medrxiv.org/content/early/2021/12/16/2021.12.15.21267884.abstract
DOI: 10.1101/2021.12.15.21267884

10. Billy JG, Kilpatrick AM. Estimates of reduced vaccine effectiveness against hospitalization, infection, transmission and symptomatic disease of a new SARS-CoV-2 variant, Omicron (B.1.1.529), using neutralizing antibody titers. 2021.
ABSTRACT: The emergence of the Omicron variant (B.1.1.529) of SARS-CoV-2 has raised concerns about how mutations in the spike protein might influence immune escape and vaccine protection against infection and disease, COVID-19. Initial estimates of immune escape measure neutralizing antibody titers, which have been shown to be a correlate of protection for COVID-19, but vary among studies. However, no studies have examined variation in vaccine effectiveness (VE) using estimated reductions in neutralizing antibody titers across virus variants. We quantified consistency in relative neutralizing antibody titers across studies. We then examined relationships between variant-specific reductions in neutralizing antibodies and protection against documented infection, symptomatic disease, and hospitalizations across variants and vaccines. We found considerable variation in variant-specific neutralizing antibody titers between studies, but within-study comparisons across variants were far more robust. There was insufficient data to estimate VE for a single vaccine across variants, especially for higher levels of immune evasion (>7-fold reductions in neutralizing antibody titers) observed with the Omicron variant (40-fold). Instead, we leveraged variation among both vaccines and virus variants to estimate VE - neutralizing antibody titer relationships across a 30 to 100-fold range of neutralizing antibody titers reduction.

Omicron increased the risk of hospitalization four to five-fold and increased the risk of symptomatic disease seven to ten-fold for mRNA vaccinees, with similar relative effects for recently vaccinated, or individuals with waned antibody titers. Third doses restored titers and protection to levels similar to waned immunity against Delta. Overall, these analyses indicate that vaccine effectiveness against severe disease is significantly diminished for waned individuals, and protection against infection, symptomatic disease and transmission is nearly eliminated. However, third doses significantly ameliorate these reductions but only restore protection to levels equivalent to waned protection against the Delta variant. The invasion of Omicron is likely to result in widespread infection, and substantial hospitalizations unless widespread boosting of immunity occurs. FundingCalifornia Department of Health, National Science Foundation
URL: https://medrxiv.org/cgi/content/short/2021.12.10.21267594

11. Blairon L, Cupaiolo R, Adriaens J, et al. Microbiology - Infectious diseases including COVID 19. Clin Chem Lab Med. 2021;59(s1):s564-s646. DOI: 10.1515/cclm-2021-5027
ABSTRACT: BACKGROUND-AIM Variants of concern (VOC) of SARS-CoV-2 are present worldwide but their distribution varies from one region to another. The Next-Generation Sequencing (NGS) is the reference method for accurately identifying VOCs. However, the NGS is expensive, time-consuming and requires expertise for interpretation. In addition, a fairly high viral load is required to achieve good performance. In recent months, it has been possible to detect the most frequent mutations of the spike protein of SARS-CoV-2 using a RT-qPCR. We present here the observations of the evolution of SARS-CoV-2 epidemiology in the region of Brussels thanks to this technique. METHODS All SARS-CoV-2 positive samples analysed by one of the molecular methods used in our laboratory were selected for identification of variants using the Allplex Variant I and Variant II Assays (Seegene Technologies, Seoul, South Korea). Those 2 assays detect the following mutations: H69/V70del, N501Y, E484K (Variant I) and K417N, K417T, L452R and W152C (Variant II). Extraction of viral RNA was performed using the STARMag Viral DNA/RNA 200 C Kit (Seegene Technologies, Seoul, South Korea) on a STARLet platform (Hamilton Company, Reno, NV, USA). The complementary DNA synthesis and the amplification were performed with a CFX96 C1000 thermal cycler (Bio Rad Laboratories, Hercules, CA, USA). RESULTS 94,624 molecular tests were performed in our lab between March 7, 2021 and August 23, 2021. After elimination of duplicates, 3,418 positive samples were tested for VOCs. At the beginning of March, the alpha variant accounted for 64% of the VOCs. The first VOC delta was detected in early May and increased over the weeks to reach 50% of VOCs by mid-June and 90.2% by the end of the observed period. CONCLUSIONS VOCs detection by RT-qPCR is an affordable alternative to NGS. It is faster (turnaround time <5 hours), about 7 times cheaper, and provides results for Ct>25. The Allplex Variant I and Variant II Assays are able to distinguish the alpha, beta, gamma, delta, delta+, epsilon, iota and B.1.525 variants. Routine use of this method allows monitoring of local epidemiology and provides additional information to clinicians. We showed that the delta variant had become the main VOC in the Brussels region by the middle of June.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34727622
DOI: 10.1515/cclm-2021-5027

12. Bushman M, Kahn R, Taylor BP, et al. Population impact of SARS-CoV-2 variants with enhanced transmissibility and/or partial immune escape. Cell. 2021. DOI: 10.1016/j.cell.2021.11.026
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ABSTRACT: Precision monitoring of antibody responses during the COVID-19 pandemic is increasingly important during large scale vaccine rollout and rise in prevalence of Severe Acute Respiratory Syndrome-related Coronavirus-2 (SARS-CoV-2) variants of concern (VOC). Equally important is defining Correlates of Protection (CoP) for SARS-CoV-2 infection and COVID-19 disease. Data from epidemiological studies and vaccine trials identified virus neutralising antibodies (Nab) and SARS-CoV-2 antigen-specific (notably RBD and S) binding antibodies as candidate CoP. In this study, we used the World Health Organisation (WHO) international standard to benchmark neutralising antibody responses and a large panel of binding antibody assays to compare convalescent sera obtained from: a) COVID-19 patients; b) SARS-CoV-2 seropositive healthcare workers (HCW) and c) seronegative HCW. The ultimate aim of this study is to identify biomarkers of humoral immunity that could be used to differentiate severe from mild or asymptomatic SARS-CoV-2 infections. Some of these biomarkers could be used to define CoP in further serological studies using samples from vaccination breakthrough and/or re-infection cases. Whenever suitable, the antibody levels of the samples studied were expressed in International Units (IU) for virus neutralisation assays or in Binding Antibody Units (BAU) for ELISA tests. In this work we used commercial and non-commercial antibody binding assays; a lateral flow test for detection of SARS-CoV-2-specific IgG/IgM; a high throughput multiplexed particle flow cytometry assay for SARS-CoV-2 Spike (S), Nucleocapsid (N) and Receptor Binding Domain (RBD) proteins); a multiplex antigen semi-automated immuno-blotting assay measuring IgM, IgA and IgG; a pseudotyped microneutralisation test (pMN) and an electroporation-dependent neutralisation assay (EDNA). Our results indicate that overall, severe COVID-19 patients showed statistically significantly higher levels of SARS-CoV-2-specific neutralising antibodies (average 1029 IU/ml) than those observed in seropositive HCW with mild or asymptomatic infections (379 IU/ml) and that clinical severity scoring, based on WHO guidelines was tightly correlated with neutralisation and RBD/S antibodies. In addition, there was a positive correlation between severity, N-antibody assays and intracellular virus neutralisation.
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ABSTRACT: Background: By August 2021, South Africa experienced three SARS-CoV-2 waves; the second and third associated with emergence of Beta and Delta variants respectively. Methods: We conducted a prospective cohort study during July 2020-August 2021 in one rural and one urban community. Mid-turbinate nasal swabs were collected twice-weekly from household members irrespective of symptoms and tested for SARS-CoV-2 using real-time reverse transcription polymerase chain reaction (rRT-PCR). Serum was collected every two months and tested for anti-SARS-CoV-2 antibodies. Results: Among 115,759 nasal specimens from 1,200 members (follow-up rate 93%), 1976 (2%) were SARS-CoV-2-positive. By rRT-PCR and serology combined, 62% (749/1200) of individuals

experienced >/=1 SARS-CoV-2 infection episode, and 12% (87/749) experienced reinfection. Of 662 PCR-confirmed episodes with available data, 15% (n=97) were associated with >/=1 symptom. Among 222 households, 200 (90%) had >/=1 SARS-CoV-2-positive individual. Household cumulative infection risk (HCIR) was 25% (213/856). On multivariable analysis, accounting for age and sex, index case lower cycle threshold value (OR 3.9, 95%CI 1.7-8.8), urban community (OR 2.0,95%CI 1.1-3.9), Beta (OR 4.2, 95%CI 1.7-10.1) and Delta (OR 14.6, 95%CI 5.7-37.5) variant infection were associated with increased HCIR. HCIR was similar for symptomatic (21/110, 19%) and asymptomatic (195/775, 25%) index cases (p=0.165). Attack rates were highest in individuals aged 13-18 years and individuals in this age group were more likely to experience repeat infections and to acquire SARS-CoV-2 infection. People living with HIV who were not virally supressed were more likely to develop symptomatic illness, and shed SARS-CoV-2 for longer compared to HIV-uninfected individuals. Conclusions: In this study, 85% of SARS-CoV-2 infections were asymptomatic and index case symptom status did not affect HCIR, suggesting a limited role for control measures targeting symptomatic individuals. Increased household transmission of Beta and Delta variants, likely contributed to successive waves, with >60% of individuals infected by the end of follow-up. Research in context: Evidence before this study: Previous studies have generated wide-ranging estimates of the proportion of SARS-CoV-2 infections which are asymptomatic. A recent systematic review found that 20% (95% CI 3%-67%) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections remained asymptomatic throughout infection and that transmission from asymptomatic individuals was reduced. A systematic review and meta-analysis of 87 household transmission studies of SARS-CoV-2 found an estimated secondary attack rate of 19% (95% CI 16-22). The review also found that household secondary attack rates were increased from symptomatic index cases and that adults were more likely to acquire infection. As of December 2021, South Africa experienced three waves of SARS-CoV-2 infections; the second and third waves were associated with circulation of Beta and Delta variants respectively. SARS-CoV-2 vaccines became available in February 2021, but uptake was low in study sites reaching 5% fully vaccinated at the end of follow up. Studies to quantify the burden of asymptomatic infections, symptomatic fraction, reinfection frequency, duration of shedding and household transmission of SARS-CoV-2 from asymptomatically infected individuals have mostly been conducted as part of outbreak investigations or in specific settings. Comprehensive systematic community studies of SARS-CoV-2 burden and transmission including for the Beta and Delta variants are lacking, especially in low vaccination settings.Added value of this study: We conducted a unique detailed COVID-19 household cohort study over a 13 month period in South Africa, with real time reverse transcriptase polymerase chain reaction (rRT-PCR) testing twice a week irrespective of symptoms and bimonthly serology. By the end of the study in August 2021, 749 (62%) of 1200 individuals from 222 randomly sampled households in a rural and an urban community in South Africa had at least one confirmed SARS-CoV-2 infection, detected on rRT-PCR and/or serology, and 12% (87/749) experienced reinfection. Symptom data were analysed for 662 rRT-PCR-confirmed infection episodes that occurred >14 days after the start of follow-up (of a total of 718 rRT-PCR-confirmed episodes), of these, 15% (n=97) were associated with one or more symptoms. Among symptomatic indvidiausl, 9% (n=9) were hospitalised and 2% (n=2) died. Ninety percent (200/222) of included households, had one or more individual infected with SARS-CoV-2 on rRT-PCR and/or serology within the household. SARS-CoV-2 infected index cases transmitted the infection to 25% (213/856) of susceptible household contacts. Index case ribonucleic acid (RNA) viral load proxied by rRT-PCR cycle threshold value was strongly predictive of household transmission. Presence of symptoms in the index case was not associated with household transmission. Household transmission was four times greater from index cases infected with Beta variant and fifteen times greater from index cases infected with Delta variant compared to wild-type infection. Attack rates were highest in individuals aged 13-18 years and individuals in this age group were more likely to experience repeat infections and to acquire SARS-CoV-2 infection within households. People living with HIV (PLHIV) who were not virally supressed were more likely to develop symptomatic illness when infected with SARS-CoV-2, and shed SARS-CoV-2 for longer when compared to HIV-uninfected individuals.Implications of all the available evidence: We found a high rate of SARS-CoV-2 infection in households in a rural community and an urban community in South Africa, with the majority of infections being asymptomatic in individuals of all ages. Asymptomatic individuals transmitted SARS-CoV-2 at similar levels to symptomatic individuals suggesting that interventions targeting symptomatic individuals such as symptom-based testing and contact tracing of individuals tested because they report symptoms may have a limited impact as control measures. Increased household transmission of Beta and Delta variants, likely contributed to recurrent waves of COVID-19, with >60% of individuals infected by the end of follow-up. Higher attack rates, reinfection and acquisition in adolescents and prolonged SARS-CoV-2 shedding in

PLHIV who were not virally suppressed suggests that prioritised vaccination of individuals in these groups could impact community transmission.
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ABSTRACT: In the studies to date, the estimated fold-drop in neutralisation titre against Omicron ranges from 2- to over 20-fold depending on the study and serum tested. Collating data from these results in a combined estimate of the drop in neutralisation titre against Omicron of 9.7-fold (95%CI 5.5-17.1). We use our previously established model to predict that six months after primary immunisation with an mRNA vaccine, efficacy for Omicron is estimated to have waned to around 40% against symptomatic and 80% against severe disease. A booster dose with an existing mRNA vaccine (even though it targets the ancestral spike) has the potential to raise efficacy for Omicron to 86.2% (95% CI: 72.6-94) against symptomatic infection and 98.2% (95% CI: 90.2-99.7) against severe infection.
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ABSTRACT: The sudden rise in COVID-19 cases in 2020 and the incessant emergence of fast-spreading variants have created an alarming situation worldwide. Besides the continuous advancements in the design and development of vaccines to combat this deadly pandemic, new variants are frequently reported, possessing mutations that rapidly outcompeted an existing population of circulating variants. As concerns grow about the effects of mutations on the efficacy of vaccines, increased transmissibility, immune escape, and diagnostic failures are few other apprehensions liable for more deadly waves of COVID-19. Although the phenomenon of antigenic drift in new variants of SARS-CoV-2 is still not validated, it is conceived that the virus is acquiring new mutations as a fitness advantage for rapid transmission or to overcome immunological resistance of the host cell. Considerable evolution of SARS-CoV-2 has been observed since its first appearance in 2019, and despite the progress in sequencing efforts to characterize the mutations, their impacts in many variants have not been analyzed. The present article provides a substantial review of literature explaining the emerging variants of SARS-CoV-2 circulating globally, key mutations in viral genome, and the possible impacts of these new mutations on prevention and therapeutic strategies currently administered to combat this pandemic. Rising infections, mortalities, and hospitalizations can possibly be tackled through mass vaccination, social distancing, better management of available healthcare infrastructure, and by prioritizing genome sequencing for better serosurveillance studies and community tracking.
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ABSTRACT: SARS-CoV-2 variant Omicron (B.1.1.529) was classified as a variant of concern (VOC) on November 26, 2021. (1, 2) The infectivity, severity, and immune evasion properties of Omicron relative to the Delta variant will determine 1) the probability of dominant future transmission, and 2) the impact on disease burden. (3, 4) Here we apply an individual-based transmission model to identify thresholds for Omicrons potential dominance, impact on health, and risk to health systems; and identify for which combinations of viral properties, current interventions would be sufficient to control transmission. We show that, with first-generation SARS-CoV-2 vaccines (5) and limited physical distancing in place, the threshold for Omicrons future dominance will primarily be driven by its degree of infectivity. However, Omicrons potential dominance may not necessarily lead to increased public health burden. Expanded vaccination that includes a third-dose for adults and child vaccination strategies is projected to have the biggest public health benefit for a highly infective, highly severe variant with low immune evasion capacity. However, a highly immune evading variant that becomes dominant will likely require alternative measures for control, such as strengthened physical distancing measures, novel treatments, and second-generation vaccines. These findings provide quantitative guidance to decision-makers at a critical time while Omicron properties are being assessed. (6) We emphasize the importance of both genomic and population epidemiological surveillance.
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had lesser contribution. Thus, the total effect of these nine mutations located on the interaction surface of RBD-hACE2 turns out to be similar to that observed in the Alpha variant. In a special circumstances it could be further altered by the E484A and S477N mutations and even lower binding capacity is likely to be detected. Finally, we provide a structural basis of the observed changes in the interactions. These data may explain only partially the observed in South Africa extremely high Omicron spread and is in support to the hypothesis for multiple mechanisms of actions involved in the transmission. Graphical abstract O_FIG O_LINKSMALLFIG WIDTH=200 HEIGHT=109 SRC="FIGDIR/small/471246v1_ufig1.gif" ALT="Figure 1"> View larger version (64K): org.highwire.dtl.DTLVardef@144d901org.highwire.dtl.DTLVardef@10310e7org.highwire.dtl.DTLVardef@4ac7dborg.highwire.dtl.DTLVardef@1870231_HPS_FORMAT_FIGEXP M_FIG C_FIG
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(T478K, and L452R) in the RBD, that is possibly increasing the infection rate. Here, using Molecular Mechanics (MM) and Monte Carlo (MC) sampling, we show that the double mutant variant of SARS-CoV-2 induced conformational change in ACE2-E37, which enhanced the electrostatic interactions by the formation of a salt-bridge with SARS-CoV-2-R403. In addition, we observed that the double mutated structure induced a significant change in the salt-bridge electrostatic interaction between RBD-T500 and ACE2-D355. Where that this interaction lost more than 70% of its value compared to its value in WT protein.
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ABSTRACT: Objective: We tested whether COVID-19 incidence and hospitalization rates during the Delta surge were inversely related to vaccination coverage among the 112 most populous counties in the United States, comprising 44 percent of the country's total population. Methods: We measured vaccination coverage as the percent of the county population fully vaccinated as of July 15, 2021. We measured COVID-19 incidence as the number of confirmed cases per 100,000 population during the 14-day period ending August 12, 2021 and hospitalization rates as the number of confirmed COVID-19 admissions per 100,000 population during the same 14-day period. Results: In log-linear regression models, a 10-percentage-point increase in vaccination coverage was associated with a 28.3% decrease in COVID-19 incidence (95% confidence interval, 16.8 - 39.7%), a 44.9 percent decrease in the rate of COVID-19 hospitalization (95% CI, 28.8 - 61.0%), and a 16.6% decrease in COVID-19 hospitalizations per 100 cases (95% CI, 8.4 - 24.8%). Inclusion of demographic covariables, as well as county-specific diabetes prevalence, did not weaken the observed inverse relationship with vaccination coverage. A significant inverse relationship between vaccination coverage and COVID-19 deaths per 100,000 during August 20 - September 16 was also observed. The cumulative incidence of COVID-19 through June 30, 2021, a potential indicator of acquired immunity due to past infection, had no significant relation to subsequent case incidence or hospitalization rates in August. Conclusion: Higher vaccination coverage was associated not only with significantly lower COVID-19 incidence during the Delta surge, but also significantly less severe cases of the disease.Public Interest SummaryWe tested whether COVID-19 incidence and hospitalization rates during the Delta variant-related surge were inversely related to vaccination coverage among the 112 most populous counties in the United States, together comprising 44 percent of the country's total population. A 10-percentage-point increase in vaccination coverage was associated with a 28.3% decrease in COVID-19 incidence, a 44.9 percent decrease in the rate of COVID-19 hospitalization, and a 16.6% decrease in COVID-19 hospitalizations per 100 cases. Inclusion of demographic covariables, as well as county-specific diabetes prevalence, did not weaken the observed inverse relationship with vaccination coverage. A significant inverse relationship between vaccination coverage and COVID-19 deaths per 100,000 during August 20 - September 16 was also observed. Higher vaccination coverage was associated not only with significantly lower COVID-19 incidence during the Delta surge, but also significantly less severe cases of the disease.
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ABSTRACT: Several SARS-CoV-2 variants have emerged since the pandemic, bringing about a renewed threat to the public. Delta variant (B.1.617.2) was first detected in October 2020 in India and was characterized as variants of concern (VOC) by WHO on May 11, 2021. Delta variant rapidly outcompeted other variants to become the dominant circulating lineages due to its clear competitive advantage. There is emerging evidence of enhanced transmissibility and reduced vaccine effectiveness (VE) against Delta variant. Therefore, it is crucial to understand the features and phenotypic effects of this variant. Herein, we comprehensively described the evaluation and features of Delta variant, summarized the effects of mutations in spike on the infectivity, transmission ability, immune evasion, and provided a perspective on efficient approaches for preventing and overcoming COVID-19.
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ABSTRACT: BACKGROUND: The Delta variant of SARS-CoV-2 is now the predominant variant worldwide. However, its transmission dynamics remain unclear. METHODS: We analyzed 405 local case-patients infected with the Delta variant of SARS-CoV-2 and temporal patterns of viral shedding identified between 22 June and 31 July 2021 in Daejeon, South Korea. RESULTS: Overall, 20% were presymptomatic at the time of epidemiological investigation. We identified six clustered outbreaks, and all were associated with indoor facilities. In 23 household contacts, the secondary attack rate was 63%. We estimated the mean serial interval as 3.26 days (95% credible interval, 2.92-3.60), and 15% (95% confidence interval, 13-18%) of cases seeded 80% of all local transmission. Analysis of the

nasopharyngeal swab samples identified virus shedding from the presymptomatic patients, and the highest viral load was observed two days after symptom onset. CONCLUSIONS: Our findings suggest that the Delta variant is highly transmissible in indoor settings and households. Rapid contact tracing, isolation of the asymptomatic contacts, strict adherence to public health measures, and increased uptake of COVID-19 vaccination including booster doses are needed to reduce the community transmission of the Delta variant.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34865022
DOI: 10.1093/infdis/jiab586

37. Hyun Goo W, Masaud S. Omicron: A heavily mutated SARS-CoV-2 variant exhibits stronger binding to ACE2 and potently escape approved COVID-19 therapeutic antibodies. 2021.
ABSTRACT: The new SARS-CoV-2 variant of concern "Omicron" was recently (Nov. 24th. 2021) spotted in South Africa and already spread around the world due to its enhanced transmissibility. The variant became conspicuous as it harbors more than thirty mutations in the spike protein with 15 mutations in the RBD region alone, potentially dampening the potency of therapeutic antibodies and enhancing the ACE2 binding. More worrying, Omicron infections have been reported in individuals who have received vaccines jabs in South Africa and Hong Kong. Here, we investigated the binding strength of Omicron with ACE2 and seven monoclonal antibodies that are either approved by FDA for COVID-19 therapy or undergoing phase III clinical trials. Computational mutagenesis and binding free energies could confirm that Omicron Spike binds ACE2 stronger than prototype SARS-CoV-2. Notably, three substitutions, i.e., T478K, Q493K, and Q498R, significantly contribute to the binding energies and doubled electrostatic potential of the RBDOmic-ACE2 complex. Instead of E484K substitution that helped neutralization escape of Beta, Gamma, and Mu variants, Omicron harbors E484A substitution. Together, T478K, Q493K, Q498R, and E484A substitutions contribute to a significant drop in the electrostatic potential energies between RBDOmic-mAbs, particularly in Etesevimab, Bamlanivimab, and CT-p59. CDR diversification could help regain the neutralization strength of these antibodies; however, we could not conduct this analysis to this end. Conclusively, our findings suggest that Omicron binds ACE2 with greater affinity, enhancing its infectivity and transmissibility. Mutations in the Spike are prudently devised by the virus that enhances the receptor binding and weakens the mAbs binding to escape the immune response.
URL: https://biorxiv.org/cgi/content/short/2021.12.04.471200

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ABSTRACT: In less than two years since SARS-CoV-2 emerged, the new coronavirus responsible for COVID-19, has accumulated a great number of mutations. Many of these mutations are located in the Spike protein and some of them confer to the virus higher transmissibility or partial resistance to antibody mediated neutralization. Viral variants with such confirmed abilities are designated by WHO as Variants of Concern (VOCs). The aim of this study was to monitor the introduction of variants and VOCs in Venezuela. A small fragment of the viral genome was sequenced for the detection of the most relevant mutations found in VOCs. This approach allowed the detection of Gamma VOC. Its presence was confirmed by complete genome sequencing. The Gamma VOC was detected in Venezuela since January 2021, and in March 2021 was predominant in the East and Central side of the country, representing more than 95% of cases sequenced in all the country in April-May 2021. In addition to the Gamma VOC, other isolates carrying the mutation E484K were also detected. The frequency of this mutation has been increasing worldwide, as shown in a survey of sequences carrying E484K mutation in GISAID, and was detected in Venezuela in many probable cases of reinfection. Complete genome sequencing of these cases allowed us to identify E484K mutation in association with Gamma VOC and other lineages. In conclusion, the strategy adopted in this study is suitable for genomic surveillance of variants for countries lacking robust genome sequencing capacities. In the period studied, Gamma VOC seems to have rapidly become the dominant variant throughout the country.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34800714
DOI: 10.1016/j.meegid.2021.105147

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ABSTRACT: We used the incidence of spike gene target failures identified during PCR testing to provide an early projection of the prevalence of severe acute respiratory syndrome coronavirus 2 variant B.1.1.7 in a university setting in Texas, USA, before sequencing results were available. Findings from a more recent evaluation validated those early projections.
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DOI: 10.3201/eid2712.210652

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ABSTRACT: B.1.1.7 is a recently discovered variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) associated with increased transmissibility. Recent findings indicate that this variant has a propensity to infect adolescents and children at higher rates than adults. The virus gains entry into various body cells utilizing angiotensin-converting enzyme 2 (ACE-2) and basigin (CD147) as receptors. The virus mainly affects type II pneumocytes of lungs, endothelial cells, enterocytes, and renal tubular cells. It is reported to affect testes, causing testicular pain, and producing histopathological changes, as observed in some autopsies. The B.1.1.7 variant can also affect various cells in the testes. This raises a major concern regarding the long-term effects of the viral infection on spermatogenesis and highlights the pressing need for a robust database of serum samples from infected male children.
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DOI: 10.1515/jbcpp-2021-0083

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ABSTRACT: Following the discovery of the SARS-CoV-2 Omicron variant (B.1.1.529), the global COVID-19 outbreak has resurfaced after appearing to be relentlessly spreading over the past 2 years. This new variant showed marked degree of mutation, compared with the previous SARS-CoV-2 variants. This study investigates the evolutionary links between Omicron variant and recently emerged SARS-CoV-2 variants. The entire genome sequences of SARS-CoV-2 variants were obtained, aligned using Clustal Omega, pairwise comparison was computed, differences, identity percent, gaps, and mutations were noted, and the identity matrix was generated. The phylogenetics of Omicron variants were determined using a variety of evolutionary substitution models. The ultrametric and metric clustering methods, such as UPGMA and neighbor-joining (NJ), using nucleotide substitution models that allowed the inclusion of nucleotide transitions and transversions as Kimura 80 models, revealed that the Omicron variant forms a new monophyletic clade that is distant from other SARS-CoV-2 variants. In contrast, the NJ method using a basic nucleotide substitution model such as Jukes-Cantor revealed a close relationship between the Omicron variant and the recently evolved Alpha variant. Based on the percentage of sequence identity, the closest variants were in the following order: Omicron, Alpha, Gamma, Delta, Beta, Mu, and then the SARS-CoV-2 USA isolate. A genome alignment with other variants indicated the greatest number of gaps in the Omicron variant's genome ranging from 43 to 63 gaps. It is possible, given their close relationship to the Alpha variety, that Omicron has been around for much longer than predicted, even though they created a separate monophyletic group. Sequencing initiatives in a systematic and comprehensive manner is highly recommended to study the evolution and mutations of the virus.
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ABSTRACT: Severe Acute Respiratory Coronavirus (SARS-CoV-2) has been emerging in the form of different variants since its first emergence in early December 2019. A new Variant of Concern (VOC) named the Omicron variant (B.1.1.529) was reported recently. This variant has a large number of mutations in the S protein. To date, there exists a limited information on the Omicron variant. Here we present the analyses of mutation distribution, the evolutionary relationship of Omicron with previous variants, and probable structural impact of mutations on antibody binding. Our analyses show the presence of 46 high prevalence mutations specific to Omicron. Twenty-

three of these are localized within the spike (S) protein and the rest localized to the other 3 structural proteins of the virus, the envelope (E), membrane (M), and nucleocapsid (N). Phylogenetic analysis showed that the Omicron is closely related to the Gamma (P.1) variant. The structural analyses showed that several mutations are localized to the region of the S protein that is the major target of antibodies, suggesting that the mutations in the Omicron variant may affect the binding affinities of antibodies to the S protein.
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DOI: 10.1016/j.jaut.2021.102779

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ABSTRACT: Severe acute respiratory syndrome coronavirus 2 Alpha and Beta variants became dominant in Finland in spring 2021 but had diminished by summer. We used phylogenetic clustering to identify sources of spreading. We found that outbreaks were mostly seeded by a few introductions, highlighting the importance of surveillance and prevention policies.
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DOI: 10.1016/S0140-6736(21)02758-6

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ABSTRACT: In late November 2021, the World Health Organization declared the SARS-CoV-2 lineage B.1.1.529 the fifth variant of concern, Omicron. This variant has acquired 15 mutations in the receptor binding domain of the spike protein, raising concerns that Omicron could evade naturally acquired and vaccine-derived immunity. We utilized an authentic virus, multicycle neutralisation assay to demonstrate that sera collected 1, 3, and 6 months post-two doses of Pfizer-BioNTech BNT162b2 has a limited ability to neutralise SARS-CoV-2. However, four weeks after a third dose, neutralizing antibody titres are boosted. Despite this increase, neutralising antibody titres are reduced 4-fold for Omicron compared to lineage A.2.2 SARS-CoV-2.
URL: https://biorxiv.org/cgi/content/short/2021.12.12.472252

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ABSTRACT: Emerging 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, WHO 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 behaviour. 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 work and found that the Omicron variant had a higher affinity for human ACE2 than the Delta variant due to a significant number of mutations in the SARS-CoV-2 receptor binding domain, 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 receptor-binding domain (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.
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DOI: 10.1002/jmv.27526

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ABSTRACT: [Figure: see text].
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ABSTRACT: It feels like the world is slowly closing in on me as I hear the ambulances pass my window at home. I remember the last time I felt this way—March 2020. News, social media, and texts from friends and work are all focused on the same thing: potential impending doom from covid-19. Except it's no longer the first, or second, or third wave. At this point, I've lost count. Omicron is coming, and I don't know if I'm ready.During the first wave in New York, covid-19 was the "novel" coronavirus and I was a "healthcare hero," sent off to fight for the lives of my patients. We had no data, no knowledge, and no experience. Covid had the upper hand and claimed the lives of tens of thousands of people in my city. Yet I would go to work each day with a mix of fear and pride: my calling as a doctor is to help when others are in need, and I was literally putting my life at risk to do so. Without medications, vaccinations, or …
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ABSTRACT: IntroductionThe SARS-CoV-2 lineages carrying the amino acid change D614G have become the dominant variants in the global COVID-19 pandemic. By June 2021, all the emerging variants of concern carried the D614G mutation. The rapid spread of the G614 mutant suggests that it may have a transmission advantage over the D614 wildtype.AimOur objective was to estimate the transmission advantage of D614G by integrating phylogenetic and epidemiological analysis.MethodsWe assume that the mutation D614G was the only site of interest which characterised the two cocirculating virus strains by June 2020, but their differential transmissibility might be attributable to a combination of D614G and other mutations. We define the fitness of G614 as the ratio of the basic reproduction number of the strain with G614 to the strain with D614 and applied an epidemiological framework for fitness inference to analyse SARS-CoV-2 surveillance and sequence data.ResultsUsing this framework, we estimated that the G614 mutant is 31% (95% credible interval: 28-34) more transmissible than the D614 wildtype. Therefore, interventions that were previously effective in containing or mitigating the D614 wildtype (e.g. in China, Vietnam and Thailand) may be less effective against the G614 mutant.ConclusionOur framework can be readily integrated into current SARS-CoV-2 surveillance to monitor the emergence and fitness of mutant strains such that pandemic surveillance, disease control and development of treatment and vaccines can be adjusted dynamically.
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DOI: 10.2807/1560-7917.ES.2021.26.49.2002005

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ABSTRACT: The Omicron (B.1.1.529) variant of SARS-CoV-2 was only recently detected in southern Africa, but its subsequent spread has been extensive, both regionally and globally1. It is expected to become dominant in the coming weeks2, probably due to enhanced transmissibility. A striking feature of this variant is the large number of spike mutations3 that pose a threat to the efficacy of current COVID-19 vaccines and antibody therapies4. This concern is amplified by the findings from our study. We found B.1.1.529 to be markedly resistant to neutralization

by serum not only from convalescent patients, but also from individuals vaccinated with one of the four widely used COVID-19 vaccines. Even serum from persons vaccinated and boosted with mRNA-based vaccines exhibited substantially diminished neutralizing activity against B.1.1.529. By evaluating a panel of monoclonal antibodies to all known epitope clusters on the spike protein, we noted that the activity of 18 of the 19 antibodies tested were either abolished or impaired, including ones currently authorized or approved for use in patients. In addition, we also identified four new spike mutations (S371L, N440K, G446S, and Q493R) that confer greater antibody resistance to 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.Competing Interest StatementL.L., S.I., M.S.N., J.Y., Y.H., and D.D.H. are inventors on patent applications on some of the antibodies described in this manuscript.
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ABSTRACT: Beginning in the summer of 2020, a variant of SARS-CoV-2, the cause of the COVID-19 pandemic, emerged in the United Kingdom. This B.1.1.7 variant, also known as Alpha, increased rapidly in prevalence, attributed to an increase in infection and/or transmission efficiency(1). The Alpha variant has 19 nonsynonymous mutations across its viral genome, including 8 substitutions or deletions in the spike protein, which interacts with cellular receptors to mediate infection and tropism. Here, using a reverse genetics approach, we show that, of the 8 individual spike protein substitutions, only N501Y exhibited consistent fitness gains for replication in the upper airway in the hamster model as well as primary human airway epithelial cells. The N501Y substitution recapitulated the phenotype of enhanced viral transmission seen with the combined 8 Alpha spike mutations, suggesting it is a major determinant of increased transmission of this variant. Mechanistically, the N501Y substitution improved the affinity of the viral spike protein for cellular receptors. As suggested by its convergent evolution in Brazil, South Africa, and elsewhere(2,3), our results indicate that N501Y substitution is a major adaptive spike mutation of major concern.
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ABSTRACT: New lineages of SARS-CoV-2 are of potential concern due to higher transmissibility, risk of severe outcomes, and/or escape from neutralizing antibodies. Lineage B.1.1.7 (the Alpha variant) became dominant in early 2021, but the association between transmissibility and risk factors, such as age of primary case and viral load remains poorly understood. Here, we used comprehensive administrative data from Denmark, comprising the full population (January 11 to February 7, 2021), to estimate household transmissibility. This study included 5,241 households with primary cases; 808 were infected with lineage B.1.1.7 and 4,433 with other lineages. Here, we report an attack rate of 38% in households with a primary case infected with B.1.1.7 and 27% in households with other lineages. Primary cases infected with B.1.1.7 had an increased transmissibility of 1.5-1.7 times that of primary cases infected with other lineages. The increased transmissibility of B.1.1.7 was multiplicative across age and viral load.
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ABSTRACT: The SARS-CoV-2 omicron variant, first detected in South Africa on 24 November, has now been found in 57 countries. Elisabeth Mahase looks at what we know about it so far, including how well treatments and vaccines workOmicron's spike protein has at least 30 amino acid substitutions, three small deletions, and one small insertion, says the US Centers for Disease Control and Prevention. The CDC has highlighted four key mutations that may aid transmission: N501Y, H655Y, N679K, and P681H, the last of which has also been found in the alpha variant, while a different mutation at this position (P681R) is found in delta.1Early indications are that omicron is

more transmissible than previous variants, especially as it has overtaken delta as the predominant variant in South Africa, and there is evidence indicating that it comes with an increased risk of reinfection.2The UK's pandemic modelling group SPI-M-O has warned that although data from South Africa are subject to caveats there is a strong indication that omicron has a "significant transmission advantage, significant immune escape, or both, or some other fitness advantage over the predominant variant (delta)." It said that the current evidence presents a "compelling case for omicron to cause a wave of infection in the UK."3England's health secretary, Sajid Javid, told Sky News on 8 December, "It spreads faster than any other covid-19 variant we've seen so far . . . We estimate [it's doubling time] is between two and a half to three days, which would mean at this rate by the end of this month we could hit about a million infections in the community throughout the UK."4It has been suggested that …
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ABSTRACT: Since its emergence in 2019 SARS-CoV-2 has proven to have a higher level of morbidity and mortality compared to the other prevailing coronaviruses. Although initially most African countries were spared from the devastating effect of SARS-CoV-2, at present almost every country has been affected. Although no association has been established between being HIV-1-infected and being more vulnerable to contracting COVID-19, HIV-1-infected individuals have a greater risk of developing severe COVID-19 and of COVID-19 related mortality. The rapid development of the various types of COVID-19 vaccines has gone a long way in mitigating the devastating effects of the virus and has controlled its spread. However, global vaccine deployment has been uneven particularly in Africa. The emergence of SARS-CoV-2 variants, such as Beta and Delta, which seem to show some subtle resistance to the existing vaccines, suggests COVID-19 will still be a high-risk infection for years. In this review we report on the current impact of COVID-19 on HIV-1-infected individuals from an immunological perspective and attempt to make a case for prioritising COVID-19 vaccination for those living with HIV-1 in Sub-Saharan Africa (SSA) countries like Malawi as one way of minimising the impact of COVID-19 in these countries.
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DOI: 10.3389/fimmu.2021.797117

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ABSTRACT: OBJECTIVE: Variants of concern (VOCs) associated with relatively high transmissibility appear to be rapidly spreading in Gabon. Therefore, it is imperative to understand the distribution of several VOCs in the population, which could have implications for transmissibility and vaccine efficacy. METHODS: Between February and May 2021, SARS-CoV-2 genomes were sequenced using the Oxford nanopore MinION method and the respective genome diversity was elucidated. Phylogenetic analysis was performed and genomes were classified using pangolin lineages. RESULTS: The results highlighted an increase (46%) in the alpha VOC (B.1.1.7) in the Gabonese population over the study period. In addition, an increase (31%) in the B.1.1.318 lineage, which is associated with high transmission and impaired vaccine efficacy (D614G+E484K+Y144del), was detected. CONCLUSION: With the second wave ongoing, these findings highlight the need for surveillance of the SARS-CoV-2 genome in the Republic of Gabon and should provide useful guidance to policymakers in selecting an appropriate vaccine for this population.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34742926
DOI: 10.1016/j.ijid.2021.10.057

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ABSTRACT: BackgroundThe ongoing COVID-19 pandemic is caused by the beta coronavirus SARS-CoV-2. COVID-19 manifests itself from mild or even asymptomatic infections to severe forms of life-threatening pneumonia. At the end of November 2021, yet another novel SARS-CoV-2 variant named B.1.1.529 or Omicron was discovered and classified as a variant of concern (VoC) by the WHO. Omicron shows significantly more mutations in the amino acid (aa) sequence of its spike protein than any previous variant, with the majority of those concentrated in the receptor binding domain (RBD). In this work, the binding of the Omicron RBD to the human ACE2 receptor was experimentally analyzed in comparison to the original Wuhan SARS-CoV-2 virus, and the Beta and Delta variants. Moreover, we compared the ability of human sera from COVID-19 convalescent donors and persons fully vaccinated with BNT162b2 (Corminaty) or Ad26.COV2.S (Janssen COVID-19 vaccine) as well as individuals who had boost vaccine doses with BNT162b2 or mRNA-1273 (Spikevax) to bind the different RBDs variants. MethodsThe Omicron RBD with 15 aa mutations compared to the original Wuhan strain was produced baculovirus-free in insect cells. Binding of the produced Omicron RBD to hACE was analyzed by ELISA. Sera from 27 COVID-19 patients, of whom 21 were fully vaccinated and 16 booster recipients were titrated on the original Wuhan strain, Beta, Delta and Omicron RBD and compared to the first WHO Integrnational Standard for anti-SARS-CoV-2 immunoglobulin (human) using the original Wuhan strain as reference. ResultsThe Omicron RBD showed a slightly reduced binding to ACE2 compared to the other RBDs. The serum of COVID-19 patients, BNT162b2 vaccinated and boost vaccinated persons showed a reduced binding to Omicron RBD in comparison to the original Wuhan strain, Beta und Delta RBDs. In this assay, the boost vaccination did not improve the RBD binding when compared to the BNT162b2 fully vaccinated group. The RBD binding of the Ad26.COV2.S serum group was lower at all compared to the other groups. ConclusionsThe reduced binding of human sera to Omicron RBD provides first hints that the current vaccinations using BNT162b2, mRNA-1273 and Ad26.COV2.S may be less efficient in preventing infections with the Omicron variant.
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ABSTRACT: The rapid spread of the SARS-CoV-2 Omicron variant suggests that the virus might become globally dominant. Further, the high number of mutations in the viral spike-protein raised concerns that the virus might evade antibodies induced by infection or vaccination. Here, we report that the Omicron spike was resistant against most therapeutic antibodies but remained susceptible to inhibition by Sotrovimab. Similarly, the Omicron spike evaded neutralization by antibodies from convalescent or BNT162b2-vaccinated individuals with 10- to 44-fold higher efficiency than the spike of the Delta variant. Neutralization of the Omicron spike by antibodies induced upon heterologous ChAdOx1/BNT162b2-vaccination or vaccination with three doses of BNT162b2 was more efficient, but the Omicron spike still evaded neutralization more efficiently than the Delta spike. These findings indicate that most therapeutic antibodies will be ineffective against the Omicron variant and that double immunization with BNT162b2 might not adequately protect against severe disease induced by this variant.
URL: https://biorxiv.org/cgi/content/short/2021.12.12.472286

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ABSTRACT: It was always a matter of when rather than if. The emergence of a new variant of SARS-CoV-2 with the ability to escape prior immunity was inevitable, given the evolutionary pressures on the virus and its ability to mutate.1 And we can already say with certainty that Omicron will not be the last variant. Indeed, there are already reports of a further mutation that undermines the ability to track Omicron by means of its signature on PCR testing—the S Gene Target Failure.2Although the evidence is still fragmentary, we have learnt a great deal about this variant in only a few weeks, not least because of the remarkable work done by some amazing South African scientists. Genome sequencing has found at least four sets of mutations causing concern—with potential to attach more strongly to cells, to reproduce more quickly, and to evade both innate and antibody-induced immunity.3 Virologists and immunologists have shown that the ability of antibodies from vaccination or prior infection are much less effective in neutralising it, although the precise estimates differ.4 Epidemiologists in South Africa and

elsewhere have shown that infections are spreading far faster than previously, with accounts of superspreading events suggesting an exceptionally high attack rate. And although some initial reports suggested that it may only cause mild infections, the analysts at South Africa's National Institute for Communicable Diseases have established an excellent surveillance system that is showing a steep increase in hospitalisations.5 Putting all of this together, those advising the British government are right to be concerned. And they have now convinced ministers to act on their warnings. The Westminster government's Plan B has finally been activated for England (many of its provisions are …
URL: https://www.ncbi.nlm.nih.gov/pubmed/34887244
DOI: 10.1136/bmj.n3055

61. Mert G, Ahmet Y, Mert G. The Omicron Variant Increases the Interactions of SARS-CoV-2 Spike Glycoprotein with ACE2. 2021.
ABSTRACT: Recently detected Omicron variant of SARS-CoV-2 (B.1.1.529) is heavily mutated on the receptor-binding domain (RBDOmicron) of its spike glycoprotein (S). RBD plays a critical role in viral infection by binding to the peptidase domain (PD) of angiotensin-converting enzyme 2 (ACE2) receptors in host cells. To investigate how Omicron mutations affect RBD-PD interactions, we performed all-atom molecular dynamics simulations of the RBDOmicron-PD in the presence of explicit water and ions. Simulations revealed that RBDOmicron exhibits a more dispersed interaction network on both sides of the RBD-PD interaction surface. Mutations resulted in an increased number of salt bridges and hydrophobic interactions between RBDOmicron and PD compared to wild-type RBD (RBDWT). Using the conformations sampled in each trajectory, the Molecular Mechanics Poisson-Boltzmann Surface Area (MMPBSA) method estimated ~44% stronger binding free energy for RBDOmicron compared to RBDWT, which may result in higher binding efficiency of the SARS-CoV-2 virus to infect host cells.
URL: https://biorxiv.org/cgi/content/short/2021.12.06.471377

62. Miller NL, Clark T, Raman R, et al. Insights on the mutational landscape of the SARS-CoV-2 Omicron variant. bioRxiv. 2021. DOI: 10.1101/2021.12.06.471499
ABSTRACT: 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 Omicronaeuros escape, and in particular advise careful surveillance of two subclades bearing R346S/K mutations. 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

63. Nariko I, Atsushi H, Yusuke H, et al. SARS-CoV-2 Omicron variant escapes neutralization by vaccinated and convalescent sera and therapeutic monoclonal antibodies. 2021.
ABSTRACT: The novel SARS-CoV-2 variant, Omicron (B.1.1.529) contains about 30 mutations in the spike protein and the numerous mutations raise the concern of escape from vaccine, convalescent sera and therapeutic drugs. Here we analyze the alteration of their neutralizing titer with Omicron pseudovirus. Sera of 3 months after double BNT162b2 vaccination exhibite [~]27-fold lower neutralization titers against Omicron than D614G mutation. Neutralization titer is also reduced in convalescent sera from Alpha and Delta patients. However, some Delta patients have relatively preserved neutralization activity up to the level of 3-month double BNT162b2 vaccination. Omicron escapes from the cocktail of imdevimab and casirivimab, whereas sotrovimab that targets the conserved region to prevent viral escape is effective to Omicron similarly to the original SARS-CoV-2. The ACE2 decoy is

another modality that neutralize the virus independently of mutational escape and Omicron is also sensitive to the engineered ACE2.
URL: https://medrxiv.org/cgi/content/short/2021.12.13.21267761

64. Oehmke TB, Moss CB, Oehmke JF. COVID-19 Surveillance Updates in U.S. Metropolitan Areas-A Dynamic Panel Data Modeling Approach: Is the 'Delta wave' over? JMIR Public Health Surveill. 2021. DOI: 10.2196/28737
ABSTRACT: BACKGROUND: Despite the availability of vaccines, the U.S. incidence of new COVID-19 cases per day nearly doubled from the beginning of July to the end of August, fueled largely by the rapid spread of the Delta variant. While the 'Delta wave' appears to have peaked nationally, some states and municipalities continue to see elevated numbers of new cases. Vigilant surveillance including at a metropolitan level can help identify any re-ignition and validate continued and strong public health policy responses in problem localities. OBJECTIVE: This surveillance report aims to provide up to date information for the 25 largest U.S. metropolitan areas about the rapidity of descent in the number of new cases following the Delta wave peak, as well as any potential re-ignition of the pandemic associated with declining vaccine effectiveness over time, new variants, or other factors. METHODS: COVID-19 pandemic dynamics for the 25 largest U.S. metropolitan areas were analyzed through Sep. 19th, 2021 using novel metrics of speed, acceleration, jerk, and 7-day persistence, calculated from observed data on the cumulative number of cases as reported in usafacts.org. Statistical analysis was conducted using dynamic panel data models estimated with Arellano-Bond regression techniques. Results are presented in tabular and graphic forms for visual interpretation. RESULTS: On average, speed in the 25 largest U.S. metropolitan areas declined from 34 new cases per day per 100,000 population during the week ending in Aug. 15th, 2021 to 29 new cases per day per 100,000 population during the week ending in Sep. 19th, 2021. This average masks important differences across metropolitan areas. For example, Miami's speed decreased from 105 for the week ending in Aug. 15th, 2021 to 40 the week ending in Sep. 19th, 2021. Los Angeles, San Francisco, Riverside, and San Diego had decreasing speed over the sample period and ended with single digit speeds for the week ending Sep. 19th, 2021. However, Boston, Washington DC, Detroit, Minneapolis, Denver, and Charlotte all had their highest speed of the sample during the week ending Sep. 19th, 2021. These cities, as well as Houston and Baltimore, had positive acceleration for the week ending Sep. 19th, 2021. CONCLUSIONS: There is great variation in epidemiological curves across U.S. metropolitan areas, including increasing numbers of new cases in eight of the largest 25 metropolitan areas for the week ending Sep. 19th, 2021. These trends, plus the possibility of waning vaccine effectiveness and the emergence of resistant variants, strongly indicates the need for continued surveillance and perhaps a return to more restrictive public health guidelines for some areas. CLINICALTRIAL: Not Applicable.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34882569
DOI: 10.2196/28737

65. Pannus P, Neven KY, De Craeye S, et al. Poor antibody response to BioNTech/Pfizer COVID-19 vaccination in SARS-CoV-2 naive residents of nursing homes. Clin Infect Dis. 2021. DOI: 10.1093/cid/ciab998
ABSTRACT: BACKGROUND: Residents of nursing homes (NH) are at high risk of COVID-19 related morbidity and death and may respond poorly to vaccination because of old age and frequent comorbidities. METHODS: Seventy-eight residents and 106 staff members, naive or previously infected with SARS-CoV-2, were recruited in NH in Belgium before immunization with two doses of 30microg BNT162b2 mRNA vaccine at day 0 and day 21. Binding antibodies (Ab) to SARS-CoV-2 receptor binding domain (RBD), spike domains S1 and S2, RBD Ab avidity, and neutralizing Ab against SARS-CoV-2 wild type and B.1.351 were assessed at days 0, 21, 28, and 49. RESULTS: SARS-CoV-2 naive residents had lower Ab responses to BNT162b2 mRNA vaccination than naive staff. These poor responses involved lower levels of IgG to all spike domains, lower avidity of RBD IgG, and lower levels of Ab neutralizing the vaccine strain. No naive resident had detectable neutralizing Ab to the B.1.351 variant. In contrast, SARS-CoV-2 infected residents had high responses to mRNA vaccination, with Ab levels comparable to infected staff. Cluster analysis revealed that poor vaccine responders not only included naive residents but also naive staff, emphasizing the heterogeneity of responses to mRNA vaccination in the general population. CONCLUSIONS: The poor Ab responses to mRNA vaccination observed in infection naive residents and in some naive staff members of NH suggest suboptimal protection against breakthrough infection, especially with variants of concern. These data support the administration of a third dose of mRNA vaccine to further improve protection of NH residents against COVID-19.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34864935

DOI: 10.1093/cid/ciab998

66. Pascarella S, Ciccozzi M, Bianchi M, et al. The Electrostatic Potential of the Omicron Variant Spike is Higher than in Delta and Delta-plus Variants: a Hint to Higher Transmissibility? J Med Virol. 2021. DOI: 10.1002/jmv.27528
ABSTRACT: A new VOC termed omicron (PANGO lineage B.1.1.529) has recently emerged in South Africa and has since then spread worldwide. A major feature of this VOC is the high number of mutations into the Spike (S) protein, much higher than any other VOC. In this study we investigate the effects of those mutations and how they apparently modulate the affinity of the RDB domain and the ACE2 receptor. We highlights an unusual high positive electrostatic potential conferred by the above mutations and speculate about its relevance for virus transmission and infectivity. This article is protected by copyright. All rights reserved.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34914120
DOI: 10.1002/jmv.27528

67. Petersen JM, Jhala D. Sequencing for COVID-19 in the Pandemic Era: What Does it Mean? American Journal of Clinical Pathology. 2021;156(Supplement_1):S140-S1. DOI: 10.1093/ajcp/aqab191.300
ABSTRACT: Introduction/Objective: SARS-CoV-2 has been developing mutations over the course of the pandemic, leading to the rise of variants. The sequencing of these variants, however, has an unclear role for the medical center providing patient treatment. Methods/Case Report: Patient specimens that were positive for the presence of SARS-CoV-2 with a cycle threshold <30 by reverse transcriptase polymerase chain reaction (RT-PCR) were sent for sequencing at the Veterans Health Administration Public Health Reference Laboratory (PHRL). Testing for SARS-CoV-2 was by RT-PCR was initially done by either the Abbott Alinity m SARS-CoV-2 assay (Chicago IL) or the Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV assay (Sunnyvale CA). All sent patient specimens had been selected by the clinical team for concern of the presence of a SARS-CoV-2 variant. Results (if a Case Study enter NA): There were a total of 8 patients (4 males and 4 females) that were sent for sequencing. The patient ages ranged from 38 to 80 years (average 58.8). The racial proportion of the 8 patients was 2 African Americans, 2 Caucasian Americans, and 4 unanswered. All were positive for SARS-CoV-2 by RT-PCR (4 Abbott assay and 4 Cepheid assay). Six of the sequenced samples showed the NextClade 20I/501Y.V1, Pango Lineage B.1.1.7, a variant first identified in the United Kingdom; four of these six patients had documentation of vaccination prior to the infection. One sequence was a NextClade 20C Pango Lineage B.1.526.1, a variant first identified in New York. The last sequence identified was a NextClade 20G, Pango Lineage B.1, a variant predominantly seen in the United States. Conclusion(s): At the present time, sequencing of SARSCoV-2 does not have a clear clinical role. However, from a public health and epidemiological point of view, sequencing has a role in SARS-CoV-2 variant tracing and detection. Vaccine protection against variant SARSCoV-2 may not be complete as some infected patients had been vaccinated.
DOI: 10.1093/ajcp/aqab191.300

68. Planas D, Saunders N, Maes P, et al. Considerable escape of SARS-CoV-2 variant Omicron to antibody neutralization. bioRxiv. 2021:2021.12.14.472630. DOI: 10.1101/2021.12.14.472630
ABSTRACT: The SARS-CoV-2 Omicron variant was first identified in November 2021 in Botswana and South Africa. It has in the meantime spread to many countries and is expected to rapidly become dominant worldwide. The lineage is characterized by the presence of about 32 mutations in the Spike, located mostly in the N-terminal domain (NTD) and the receptor binding domain (RBD), which may enhance viral fitness and allow antibody evasion. Here, we isolated an infectious Omicron virus in Belgium, from a traveller returning from Egypt. We examined its sensitivity to 9 monoclonal antibodies (mAbs) clinically approved or in development, and to antibodies present in 90 sera from COVID-19 vaccine recipients or convalescent individuals. Omicron was totally or partially resistant to neutralization by all mAbs tested. Sera from Pfizer or AstraZeneca vaccine recipients, sampled 5 months after complete vaccination, barely inhibited Omicron. Sera from COVID-19 convalescent patients collected 6 or 12 months post symptoms displayed low or no neutralizing activity against Omicron. Administration of a booster Pfizer dose as well as vaccination of previously infected individuals generated an anti-Omicron neutralizing response, with titers 5 to 31 fold lower against Omicron than against Delta. Thus, Omicron escapes most therapeutic monoclonal antibodies and to a large extent vaccine-elicited antibodies.Competing Interest StatementC.P., H.M., O.S, T.B., F.R. have a pending patent application for an anti-RBD mAb not used in this study (PCT/FR2021/070522).

URL: http://biorxiv.org/content/early/2021/12/15/2021.12.14.472630.abstract
DOI: 10.1101/2021.12.14.472630

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URL: https://www.ncbi.nlm.nih.gov/pubmed/34896326
DOI: 10.1016/j.tmaid.2021.102234

70. Prashant R, Neha, Chandra D, et al. The influence of new SARS-CoV-2 variant Omicron (B.1.1.529) on vaccine efficacy, its correlation to Delta Variants: a computational approach. 2021.
ABSTRACT: The newly discovered COVID variant B.1.1.529 in Botswana has more than 30 mutations in spike and many other in non-spike proteins, far more than any other SARS-CoV-2 variant accepted as a variant of concern by the WHO and officially named Omicron, and has sparked concern among scientists and the general public. Our findings provide insights into structural modification caused by the mutations in the Omicrons receptor-binding domain and look into the effects on interaction with the hosts neutralising antibodies CR3022, B38, CB6, P2B-2F6, and REGN, as well as ACE2R using an in silico approach. We have employed secondary structure prediction, structural superimposition, protein disorderness, molecular docking, and MD simulation to investigate host-pathogen interactions, immune evasion, and transmissibility caused by mutations in the RBD region of the spike protein of the Omicron variant and compared it to the Delta variants (AY.1, AY.2, & AY.3) and wild type. Computational analysis revealed that the Omicron variant has a higher binding affinity for the human ACE2 receptor than the wild and Delta (AY.1 and AY.2 strains), but lower than the Delta AY.3 strain. MD simulation and docking analysis suggest that the omicron and Delta AY.3 were found to have relatively unstable and compact RBD structures and hampered interactions with antibodies more than wild and Delta (AY.1 and AY.2), which may lead to relatively more pathogenicity and antibody escape. In addition, we observed lower binding affinity of Omicron for human monoclonal antibodies (CR3022, B38, CB6, and P2B2F6) when compared to wild and Delta (AY.1 & AY.2). However, the binding affinity of Omicron RBD variants for CR3022, B38, and P2B2F6 antibodies is lower as compared to Delta AY.3, which might promote immune evasion and reinfection and needs further experimental investigation.
URL: https://biorxiv.org/cgi/content/short/2021.12.06.471215

71. Pulliam JRC, van Schalkwyk CGNvGACCGMJ, Dushoff JMKMH. Increased risk of SARS-CoV-2 reinfection associated with emergence of the Omicron variant in South Africa. 2021.
ABSTRACT: Objective To examine whether SARS-CoV-2 reinfection risk has changed through time in South Africa, in the context of the emergence of the Beta, Delta, and Omicron variantsDesign Retrospective analysis of routine epidemiological surveillance dataSetting Line list data on SARS-CoV-2 with specimen receipt dates between 04 March 2020 and 27 November 2021, collected through South Africa's National Notifiable Medical Conditions Surveillance SystemParticipants 2,796,982 individuals with laboratory-confirmed SARS-CoV-2 who had a positive test result at least 90 days prior to 27 November 2021. Individuals having sequential positive tests at least 90 days apart were considered to have suspected reinfections.Main outcome measures Incidence of suspected reinfections through time;comparison of reinfection rates to the expectation under a null model (approach 1);empirical estimates of the time-varying hazards of infection and reinfection throughout the epidemic (approach 2)Results 35,670 suspected reinfections were identified among 2,796,982 individuals with laboratory-confirmed SARS-CoV-2 who had a positive test result at least 90 days prior to 27 November 2021. The number of reinfections observed through the end of the third wave 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: 0.75 (CI95: 0.59–0.97);for wave 3 versus wave 1: 0.71 (CI95: 0.56–0.92)). In contrast, the recent spread of the Omicron variant has been associated with a decrease in the hazard coefficient for primary infection and an increase in reinfection hazard coefficient. The estimated hazard ratio for reinfection versus primary infection for the period from 1 November 2021 to 27 November 2021 versus wave 1 was 2.39 (CI95: 1.88–3.11).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. Urgent questions remain regarding whether Omicron is also able to evade vaccine-induced immunity and the potential implications of reduced immunity to infection on protection against severe disease and death.Box 1What is already known on this topicWhat is already known on this topicPrior infection with SARS-CoV-2 is estimated to provide at least an 80% reduction in infection risk (1,2).Laboratory-based studies indicate reduced neutralization by convalescent serum for the Beta and Delta variants relative to wild type virus (3–6);however, the impact of these reductions on risk of reinfection is not known, and laboratory assessments of Omicron are still underway.What this study addsWhat this study addsWe provide two methods for monitoring reinfection trends to identify signatures of changes in reinfection risk.We find no evidence of increased reinfection risk associated with circulation of Beta or Delta variants compared to the ancestral strain in routine epidemiological data from South Africa.In contrast, we find clear, population-level evidence to suggest substantial immune evasion by the Omicron variant.One sentence summary Analysis of routine surveillance data from South Africa suggests that, in contrast to the Beta and Delta, the Omicron variant of SARS-CoV-2 demonstrates substantial population-level evidence for evasion of immunity from prior infection.Competing Interest StatementAll authors have completed the ICMJE uniform iscl sure 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 StatementThis work was supported by the South African Department of Science and Innovation and the National Research Foundation and the Wellcome Trust (grant number 221003/Z/20/Z) in collaboration with the Foreign, Commonwealth and Development Office, United Kingdom.Author DeclarationsI confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained.YesThe details of the IRB/oversight body that provided approval or exemption for the research described are given below:This study has received ethical clearance from University of the Witwatersrand (Clearance certificate number M210752, formerly M160667) and approval under reciprocal review from Stellenbosch University (Project ID 19330, Ethics Reference Number N20/11/074_RECIP_WITS_M160667_COVID-19).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.YesI 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).YesI 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.YesData and code will be made available at https://github.com/jrcpulliam/reinfections. The following data are included in the repository: - Counts of reinfections and primary infections by province, age group (5-year bands), and sex (M, F, U) - Daily time series of primary infections and suspected reinfections by specimen receipt date (national) - Model output: posterior samples from the MCMC fitting procedure and simulation results Requests for additional data must be made in writing to the National Institute for Communicable Diseases, South Africa.
https://github.com/jrcpulliam/reinfections
URL: https://doi.org/10.1101/2021.11.11.21266068
DOI: 10.1101/2021.11.11.21266068

72. Qiu H, Yuan XY, Cabral T, et al. Development and characterization of SARS-CoV-2 variant-neutralizing monoclonal antibodies. Antiviral Res. 2021;196:105206. DOI: 10.1016/j.antiviral.2021.105206
ABSTRACT: Vaccination and administration of monoclonal antibody cocktails are effective tools to control the progression of infectious diseases and to terminate pandemics such as COVID-19. However, the emergence of SARS-CoV-2 mutants with enhanced transmissibility and altered antigenicity requires broad-spectrum therapies. Here we developed a panel of SARS-CoV-2 specific mouse monoclonal antibodies (mAbs), and characterized them based on ELISA, Western immunoblot, isotyping, and virus neutralization. Six neutralizing mAbs that exhibited

high-affinity binding to SARS-CoV-2 spike protein were identified, and their amino acid sequences were determined by mass spectrometry. Functional assays confirmed that three mAbs, F461G11, F461G15, and F461G16 neutralized four variants of concern (VOC): B.1.1.7 (alpha), B.1.351 (beta), P.1 (gamma) and B.1.617.2 (delta) These mAbs are promising candidates for COVID-19 therapy, and understanding their interactions with virus spike protein should support further vaccine and antibody development.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34762975
DOI: 10.1016/j.antiviral.2021.105206

73. Ramazzotti D, Maspero D, Angaroni F, et al. Early detection and improved genomic surveillance of SARS-CoV-2 variants from deep sequencing data. medRxiv. 2021:2021.12.14.21267810. DOI: 10.1101/2021.12.14.21267810
ABSTRACT: In the definition of fruitful strategies to contrast the worldwide diffusion of SARS-CoV-2, maximum efforts must be devoted to the early detection of dangerous variants. An effective help to this end is granted by the analysis of deep sequencing data of viral samples, which are typically discarded after the creation of consensus sequences. Indeed, only with deep sequencing data it is possible to identify intra-host low-frequency mutations, which are a direct footprint of mutational processes that may eventually lead to the origination of functionally advantageous variants. Accordingly, a timely and statistically robust identification of such mutations might inform political decision-making with significant anticipation with respect to standard analyses based on consensus sequences. To support our claim, we here present the largest study to date of SARS-CoV-2 deep sequencing data, which involves 220,788 high quality samples, collected over 20 months from 137 distinct studies. Importantly, we show that a relevant number of spike and nucleocapsid mutations of interest associated to the most circulating variants, including Beta, Delta and Omicron, might have been intercepted several months in advance, possibly leading to different public-health decisions. In addition, we show that a refined genomic surveillance system involving high- and low-frequency mutations might allow one to pinpoint possibly dangerous emerging mutation patterns, providing a data-driven automated support to epidemiologists and virologists.Competing Interest StatementThe authors have declared no competing interest.Funding StatementThis work was partially supported by the Elixir Italian Chapter and the SysBioNet project, a Ministero dell'Istruzione, dell'Universita' e della Ricerca initiative for the Italian Roadmap of European Strategy Forum on Research Infrastructures and by the Associazione Italiana per la Ricerca sul Cancro (AIRC)-IG grant 22082. DR and FA were partially supported by a Bicocca 2020 Starting Grant. DR was also supported by a Premio Giovani Talenti of the University of Milan-Bicocca.Author DeclarationsI confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained.YesI 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.YesI 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.YesAll data analyzed in this study are available online at the National Center for Biotechnology Information (NCBI) or the European Nucleotide Archive (ENA).
URL: http://medrxiv.org/content/early/2021/12/16/2021.12.14.21267810.abstract
DOI: 10.1101/2021.12.14.21267810

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ABSTRACT: As of September 2021, there has been a total of 123,633 confirmed cases of pregnant women with SARS-CoV-2 infection in the US according to the CDC, with maternal death being 2.85 times more likely, pre-eclampsia 1.33 times more likely, preterm birth 1.47 times more likely, still birth 2.84 times more likely, and NICU admission 4.89 times more likely when compared to pregnant women without COVID-19 infection. In our literature review, we have identified eight key changes in the immunological functioning of the pregnant body that may predispose the pregnant patient to both a greater susceptibility to SARS-CoV-2, as well as a more severe disease

course. Factors that may impede immune clearance of SARS-CoV-2 include decreased levels of natural killer (NK) cells, Th1 CD4+ T cells, plasmacytoid dendritic cells (pDC), a decreased phagocytic index of neutrophil granulocytes and monocytes, as well as the immunomodulatory properties of progesterone, which is elevated in pregnancy. Factors that may exacerbate SARS-CoV-2 morbidity through hyperinflammatory states include increases in the complement system, which are linked to greater lung injury, as well as increases in TLR-1 and TLR-7, which are known to bind to the virus, leading to increased proinflammatory cytokines such as IL-6 and TNF-alpha, which are already elevated in normal pregnant physiology. Other considerations include an increase in angiotensin converting enzyme 2 (ACE2) in the maternal circulation, leading to increased viral binding on the host cell, as well as increased IL-6 and decreased regulatory T cells in pre-eclampsia. We also focus on how the Delta variant has had a concerning impact on SARS-CoV-2 cases in pregnancy, with an increased case volume and proportion of ICU admissions among the infected expecting mothers. We propose that the effects of the Delta variant are due to a combination of (1) the Delta variant itself being more transmissible, contagious, and efficient at infecting host cells, (2) initial evidence pointing to the Delta variant causing a significantly greater viral load that accumulates more rapidly in the respiratory system, (3) the pregnancy state being more susceptible to SARS-CoV-2 infection, as discussed in-depth, and (4) the lower rates of vaccination in pregnant women compared to the general population. In the face of continually evolving strains and the relatively low awareness of COVID-19 vaccination for pregnant women, it is imperative that we continue to push for global vaccine equity.
URL: https://www.mdpi.com/2036-7449/13/4/91
DOI: 10.3390/idr13040091

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ABSTRACT: 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.
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ABSTRACT: INTRODUCTION: COVID-19 is an international public health crisis with more than 132 million infections worldwide. Beyond acute infection, emerging data indicate patients diagnosed with COVID-19 may experience

persistent sequelae similar to survivors of sepsis or acute respiratory syndromes, including mobility limitations and fatigue. However, there is limited evidence on the trajectory of functional recovery in those hospitalised with COVID-19. The primary aim of the Coronavirus Registry Functional Recovery (COREG-FR) study is to understand the trajectory of functional recovery among individuals hospitalised for COVID-19 over the medium (up to 6 months) and longer term (6-12 months) that will guide clinical care and optimal management of serious COVID-19 illness and recovery. METHODS AND ANALYSIS: COREG-FR is a multicentre longitudinal cohort study. We will enrol a minimum of 211 adults age 18 years and older with COVID-19 from five hospitals. Participants will be followed from admission to hospital as an inpatient, to hospital discharge, and at 3-month, 6-month, 9-month and up to 12-month post-hospital discharge. We will conduct telephone interviews at ward admission and discharge, and telephone interviews plus in-person assessments of physical function and lung function at all remaining follow-ups. Our primary outcome is the Activity Measure for Post-Acute Care mobility scale measured at all time points. We will conduct linear mixed effects regression analyses to explore determinants of functional outcomes after COVID-19 illness. Subgroup analyses based on age (</=65 vs >65 years), frailty status (Clinical Frailty Scale score </=4 vs >5) and variants of concern will be conducted. ETHICS AND DISSEMINATION: COREG-FR has been approved by Research Ethics Boards at participating sites. We will disseminate this work through peer-reviewed manuscripts, presentations at national and international meetings and through the established COREG website (www.coregontario.ca). COREG-FR is designed as a data platform for future studies evaluating COVID-19 recovery. TRIAL REGISTRATION NUMBER: NCT04602260; Pre-results.
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ABSTRACT: We estimated mean serial interval and superspreading potential for the Delta variant of severe acute respiratory syndrome coronavirus 2 in South Korea. Intervals were similar for the first (3.7 days) and second (3.5 days) study periods. Risk for superspreading events was also similar; 23% and 25% of cases, respectively, seeded 80% of transmissions.
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ABSTRACT: Coronavirus disease (COVID-19) caused by the SARSCoV-2 virus has exposed clinical laboratories to unprecedented challenges. With surging case numbers, clinical laboratories were forced to acquiesce and integrate multiple testing platforms with varying workflows and analytical sensitivities in order to meet testing volumes. Now a new challenge has emerged with the evolution of viral variants, both globally and locally, raising concerns for uncontrolled spread, increased disease severity, and weakened responses to vaccinations. Preliminary data suggests that these variants may be associated with higher viral titers and prolonged infections. While primarily leveraged for epidemiologic surveillance, the clinical utility of variant detection may quickly become paramount. Furthermore, laboratories must remain vigilant and nimble enough to pivot should variant identification play a role in the patient care. To prepare for the validation of clinical assays that identify important viral variants, we designed a novel method, termed VariantDirect, to screen SARS-CoV-2 positive samples for the presence of variants, focusing initially on the increasingly prevalent UK and South African (SA) variants. The detection strategy is based on primers designed to specifically target the viral receptor-binding domain mutation, N501Y, shared by the UK and SA strains. Screening for variants will be limited to nasopharyngeal swab samples of high viral titers (Ct values <25 by RT-qPCR assay, Roche Diagnostics). Pools of 9 different samples, 50 mul each, are mixed and stored at-80degreeC along with aliquots of the 9 original samples. These pools will then be tested, and if positive for the N501Y variant, the pooled 9 samples will be thawed and tested separately to identify the affected specimen. Most of these specimens are also being independently sequenced via a comprehensive but more resource-intensive NGS approach. Advantages of our pooled workflow are primarily in time and cost, with the capacity of screening up to 837 specimens on a single run. In addition, our collection strategy establishes a "time capsule" to document the evolution of viral strains within our geographical region. Finally, these studies serve to optimize technical

parameters for the development of clinical assays. A validated nucleic acid (NA) extraction-free RT-qPCR method will be utilized for this assay. Our internal validation data showed comparable analytical sensitivities to NA extraction-based methods. Pooled samples in transport medium are diluted in normal saline at a ratio of 1:1, and then heat-inactivated in the presence of proteinase-K and ultimately analyzed on the Applied BiosystemsTM 7500 Fast Dx instrument. As new variants of interest emerge, primers and probes can be quickly redesigned and validated on clinical samples within our NGS-confirmed "time capsule". This study will provide important information needed for current or future genomic and epidemiologic studies.
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ABSTRACT: The emergence of the SARS-CoV-2 Omicron variant, first identified in South Africa, may compromise the ability of vaccine and previous infection (1) elicited immunity to protect against new infection. Here we investigated whether Omicron escapes antibody neutralization elicited by the Pfizer BNT162b2 mRNA vaccine in people who were vaccinated only or vaccinated and previously infected. We also investigated whether the virus still requires binding to the ACE2 receptor to infect cells. We isolated and sequence confirmed live Omicron virus from an infected person in South Africa. We then compared neutralization of this virus relative to an ancestral SARS-CoV-2 strain with the D614G mutation. Neutralization was by blood plasma from South African BNT162b2 vaccinated individuals. We observed that Omicron still required the ACE2 receptor to infect but had extensive escape of Pfizer elicited neutralization. However, 5 out of 6 of the previously infected, Pfizer vaccinated individuals, all of them with high neutralization of D614G virus, showed residual neutralization at levels expected to confer protection from infection and severe disease (2). While vaccine effectiveness against Omicron is still to be determined, these data support the notion that high neutralization capacity elicited by a combination of infection and vaccination, and possibly by boosting, could maintain reasonable effectiveness against Omicron. If neutralization capacity is lower or wanes with time, protection against infection is likely to be low. However, protection against severe disease, requiring lower neutralization levels and involving T cell immunity, would likely be maintained.
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ABSTRACT: The SARS-CoV-2 pandemic has impacted public health systems all over the world. The Delta variant seems to possess enhanced transmissibility, but no clear evidence suggests it has increased virulence. Our data show that pre-exposed individuals had similar neutralizing activity against the authentic COVID-19 strain and the Delta and Epsilon variants. After only one vaccine dose, the neutralization capacity expanded to all tested variants in pre-exposed individuals. Healthy vaccinated individuals showed a limited breadth of neutralization. One vaccine dose did induce similar neutralizing antibodies against the Delta as against the authentic strain. However, even after two doses, this capacity only expanded to the Epsilon variant.
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ABSTRACT: BACKGROUND: Since its inception in late 2019, SARS-CoV-2 has been evolving continuously by procuring mutations, leading to emergence of numerous variants, causing second wave of pandemic in many countries including India in 2021. To control this pandemic continuous mutational surveillance and genomic epidemiology of circulating strains is very important to unveil the emergence of the novel variants and also monitor the evolution of existing variants. METHODS: SARS-CoV-2 sequences were retrieved from GISAID database. Sequence alignment was performed with MAFT version 7. Phylogenetic tree was constructed by using MEGA (version X) and UShER. RESULTS: In this study, we reported the emergence of a novel variant of SARS-CoV-2, named B.1.1.526, in India. This novel variant encompasses 129 SARS-CoV-2 strains which are characterized by the

presence of 11 coexisting mutations including D614G, P681H, and V1230L in S glycoprotein. Out of these 129 sequences, 27 sequences also harbored E484K mutation in S glycoprotein. Phylogenetic analysis revealed strains of this novel variant emerged from the GR clade and formed a new cluster. Geographical distribution showed, out of 129 sequences, 126 were found in seven different states of India. Rest 3 sequences were observed in USA. Temporal analysis revealed this novel variant was first collected from Kolkata district of West Bengal, India. CONCLUSIONS: The D614G, P618H and E484K mutations have previously been reported to favor increased transmissibility, enhanced infectivity, and immune invasion, respectively. The transmembrane domain (TM) of S2 subunit anchors S glycoprotein to the virus envelope. The V1230L mutation, present within the TM domain of S glycoprotein, might strengthen the interaction of S glycoprotein with the viral envelope and increase S glycoprotein deposition to the virion, resulting in more infectious virion. Therefore, the new variant having D614G, P618H, V1230L, and E484K may have higher infectivity, transmissibility, and immune invasion characteristics, and thus need to be monitored closely.
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ABSTRACT: 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 its implications including 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, fifteen of these mutations reside in the receptor-binding domain (RBD) of spike glycoprotein, which may alter transmissibility, infectivity, neutralizing antibody escape and vaccine breakthrough cases of COVID-19. Therefore, our present study characterizes our understanding of the current global prevalence and mutational hotspots of the Omicron variant in comparison with the Delta variant of SARS-CoV-2. Further, detailed information was analyzed to characterize the global perspective of Omicron, including mutational hotspot, transmission dynamic, effect on testing and immunity, which shall promote the progress of clinical application and basic research. Collectively, our data suggests that due to continuous variation in the spike glycoprotein structures, 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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ABSTRACT: OBJECTIVES: To study the epidemiological and clinical features of children with coronavirus disease 2019 (COVID-19) caused by Delta variant infection and their differences from children with ordinary COVID-19 (non-Delta variant infection). METHODS: Eleven children aged <14 years, who were diagnosed with COVID-19 caused by Delta variant infection from August to September 2021 were enrolled (variant group). Five children aged <14 years who were diagnosed with ordinary COVID-19 from February to March 2020 served as the control group. The epidemiological data, clinical features, and laboratory examination results were compared between the two groups. RESULTS: There was no significant difference in the proportion of children with clinical symptoms between the two groups (P>0.05). There were no significant differences in white blood cell count, lymphocyte count, and platelet count between the two groups (P>0.05), while the variant group had a lower neutrophil count than the control group (P<0.05). Lymphocytopenia was not observed in either group. Compared with the control group, the variant group had a higher proportion of children with an increase in creatine kinase isoenzyme (P<0.05), while there were no significant differences in the proportion of children with an increase in lactate dehydrogenase, D-Dimer, C-reactive protein or interleukin-6 between the two groups (P>0.05). Among the 9 children in the variant group, 5 tested positive for IgM antibody at week 2 after admission, and all children tested positive for IgG antibody. At week 3 after admission, the level of IgM antibody tended to decrease in 9 children, and the level of IgG antibody tended to decrease in 8 children. CONCLUSIONS: Delta variant is more infectious. COVID-19 caused

by Delta variant infection may cause more serious myocardial damage than ordinary COVID-19 in children. In children infected with Delta variant, IgG antibody appears at almost the same time as IgM antibody.
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ABSTRACT: Isolation guidelines for severe acute respiratory syndrome-cornavirus-2 (SARS-CoV-2) are largely derived from data collected prior to emergence of the delta variant. We followed a cohort of ambulatory patients with post-vaccination breakthrough SARS-CoV-2 infections with longitudinal collection of nasal swabs for SARS-CoV-2 viral load quantification, whole genome sequencing, and viral culture. All delta variant infections (10/10, 100%) in our cohort were symptomatic, compared with 64% (9/14) of non-delta variant infections. Symptomatic delta variant breakthrough infections were characterized by higher initial viral load, longer duration of virologic shedding by PCR, greater likelihood of replication-competent virus at early stages of infection, and longer duration of culturable virus compared to non-delta variants. The duration of time since vaccination was also correlated with both duration of PCR positivity and duration of detection of replication-competent virus. Nonetheless, no individuals with symptomatic delta variant infections had replication-competent virus by day 10 after symptom onset or 24 hours after resolution of symptoms. These data support current US Center for Disease Control isolation guidelines and reinforce the importance of prompt testing and isolation among symptomatic individuals with delta variant breakthrough infections. Additional data are needed to evaluate these relationships among asymptomatic and more severe delta variant breakthrough infections.
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ABSTRACT: Background: SARS-CoV-2 variant Beta (B.1.351) was designated as a Variant of Concern (VoC) after becoming the dominant strain in South Africa and spreading internationally. BNT162b2 showed lower levels of neutralizing antibodies against Beta than against other strains raising concerns about effectiveness of vaccines against infections caused by Beta. We estimated BNT162b2 vaccine effectiveness (VE) against Beta infections in Israel, a country with high vaccine uptake. Methods: The Ministry of Health (MoH) identified Beta cases through mandatory reporting of SARS-CoV-2 cases and whole genome sequencing (WGS) of specimens from vaccination-breakthrough infections, reinfections, arriving international travelers, and a selection of other infected persons. A cohort analysis was conducted of exposure events of contacts of primary Beta cases. WGS was conducted on available PCR-positive specimens collected from contacts. VE estimates with 95% confidence intervals (CIs) against confirmed and probable Beta infections were determined by comparing infection risk between unvaccinated and fully-vaccinated (>/=7 days after the second dose) contacts, and between unvaccinated and partially-vaccinated (<7 days after the second dose) contacts. Findings: MoH identified 310 Beta cases through Jun 27, 2021. During the study period (Dec 11, 2020 - Mar 25, 2021), 164 non-institutionalized primary Beta cases, with 552 contacts aged >/=16 years, were identified. 343/552 (62%) contacts were interviewed and tested. 71/343 (21%) contacts were PCR-positive. WGS was performed on 7/71 (10%) PCR-positive specimens; all were Beta. Among SARS-CoV-2-infected contacts, 48/71 (68%) were symptomatic, 10/71 (14%) hospitalized, and 2/71 (3%) died. Fully-vaccinated VE against confirmed or probable Beta infections was 72% (95% CI -5 - 97%; p=0.04) and against symptomatic confirmed or probable Beta infections was 100% (95% CI 19 - 100%; p=0.01). There was no evidence of protection in partially-vaccinated contacts. Interpretation: In a prospective observational study, two doses of BNT162b2 were effective against confirmed and probable Beta infections. Through the end of June 2021, introductions of Beta did not interrupt control of the pandemic in Israel. Funding: Israel Ministry of Health and Pfizer.
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ABSTRACT: The SARS-CoV-2 alpha VOC (also known as lineage B.1.1.7) initially described in the autumn, 2020 in UK, rapidly became the dominant lineage across much of Europe. Despite multiple studies reporting molecular evidence suggestive of its circulation in Brazil, much is still unknown about its genomic diversity in the state of Sao Paulo, the main Brazilian economic and transportation hub. To get more insight regarding its transmission dynamics into the State we performed phylogenetic analysis on all alpha VOC strains obtained between February and August 2021 from the Sao Paulo state Network for Pandemic Alert of Emerging SARS-CoV-2 variants. The performed phylogenetic analysis showed that most of the alpha VOC genomes were interspersed with viral strains sampled from different Brazilian states and other countries suggesting that multiple independent Alpha VOC introductions from Brazil and overseas have occurred in the Sao Paulo State over time. Nevertheless, large monophyletic clusters were also observed especially from the Central-West part of the Sao Paulo State (the city of Bauru) and the metropolitan region of the Sao Paulo city. Our results highlight the Alpha VOC molecular epidemiology in the Sao Paulo state and reinforce the need for continued genomic surveillance strategies for the real-time monitoring of potential emerging SARS-CoV-2 variants during the ever-growing vaccination process.
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ABSTRACT: The rapid spread of the Delta variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) became a serious concern worldwide in summer 2021. We examined the copy number and variant types of all SARS-CoV-2-positive patients who visited our hospital from February to August 2021 using polymerase chain reaction (PCR) tests. Whole genome sequencing was performed for some samples. The R.1 variant (B.1.1.316) was responsible for most infections in March, replacing the previous variant (B.1.1.214); the Alpha (B.1.1.7) variant caused most infections in April and May; and the Delta variant (B.1.617.2) was the most prevalent in July and August. There was no significant difference in the copy numbers among the previous variant cases (n = 29, median 3.0 x 10(4) copies/microl), R.1 variant cases (n = 28, 2.1 x 10(5) copies/microl), Alpha variant cases (n = 125, 4.1 x 10(5) copies/microl), and Delta variant cases (n = 106, 2.4 x 10(5) copies/microl). Patients with Delta variant infection were significantly younger than those infected with R.1 and the previous variants, possibly because many elderly individuals in Tokyo were vaccinated between May and August. There was no significant difference in mortality among the four groups. Our results suggest that the increased infectivity of Delta variant may be caused by factors other than the higher viral loads. Clarifying these factors is important to control the spread of Delta variant infection.
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ABSTRACT: A new variant of SARS-CoV-2 (the virus that causes COVID-19), B.1.1.529 (Omicron) (1), was first reported to the World Health Organization (WHO) by South Africa on November 24, 2021. Omicron has numerous mutations with potential to increase transmissibility, confer resistance to therapeutics, or partially escape infection- or vaccine-induced immunity (2). On November 26, WHO designated B.1.1.529 as a variant of concern (3), as did the U.S. SARS-CoV-2 Interagency Group (SIG)* on November 30. On December 1, the first case of COVID-19 attributed to the Omicron variant was reported in the United States. As of December 8, a total of 22 states had identified at least one Omicron variant case, including some that indicate community transmission. Among 43 cases with initial follow-up, one hospitalization and no deaths were reported. This report summarizes U.S. surveillance for SARS-CoV-2 variants, characteristics of the initial persons investigated with COVID-19 attributed to the Omicron variant and public health measures implemented to slow the spread of Omicron in the United States. Implementation of concurrent prevention strategies, including vaccination, masking, increasing ventilation, testing,

quarantine, and isolation, are recommended to slow transmission of SARS-CoV-2, including variants such as Omicron, and to protect against severe illness and death from COVID-19.
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ABSTRACT: “Plan B” restrictions will be implemented in England from 10 December in an attempt to slow the spread of the omicron variant, which is now present in every part of the UK, with case numbers doubling every two to three days.The prime minister announced the measures, which include mandatory mask wearing in most public indoor settings, vaccine passports for large capacity events, and working from home, during a televised press conference on 8 December. Although the measures were “irritating,” Boris Johnson said, they were the best way to ensure a “Christmas as close to normal as possible,” given that omicron seemed to be more transmissible than the previous delta variant and case numbers were “growing much faster.”And with covid hospital admissions in South Africa doubling in a week, “we can’t yet assume omicron is less severe than previous variants,” Johnson added.Although working from home is being encouraged, people will still be able to socialise freely, including at work Christmas parties.Chaand Nagpaul, the BMA’s chair of council, said that the government’s decision to implement Plan B was “the right one.”“We …
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ABSTRACT: Omicron variants are part of the "Coronavirus disease 2019 [COVID-19] Variants of Concerns" and has the potential to spread around the world rapidly and can harm human life. We can anticipate that the endemic state of COVID-19 will be characterized by the development of new strains with surges that will predominate in unvaccinated and immunodeficient populations. Thus, there will be an important role in promoting vaccinations, boosters and accessible testing to prevent disease transmission and to rapidly detect surges. There is an urgent need to explore the virology and biology of Omicron variants, define clinical phenomes and therapies, monitor dynamics of genetic changes, and translate the knowledge of COVID-19 into new variants. Clinical and translational medicine will be impactful in addressing these challenges by providing new insights for understanding and

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DOI: 10.1002/ctm2.680

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ABSTRACT: OBJECTIVES: Importations of novel variants of concern (VOC), particularly B.1.617.2, have become the impetus behind recent outbreaks of SARS-CoV-2. Concerns around the impact on vaccine effectiveness, transmissibility and severity are now driving the public health response to these variants. This paper analyses the patterns of growth in hospitalisations and confirmed cases for novel VOCs by age groups, geography and ethnicity in the context of changing behaviour, non-pharmaceutical interventions (NPIs) and the UK vaccination programme. We seek to highlight where strategies have been effective and periods that have facilitated the establishment of new variants. DESIGN: We have algorithmically linked the most complete testing and hospitalisation data in England to create a data set of confirmed infections and hospitalisations by SARS-CoV-2 genomic variant. We have used these linked data sets to analyse temporal, geographic and demographic distinctions. SETTING AND PARTICIPANTS: The setting is England from October 2020 to July 2021. Participants included all COVID-19 tests that included RT-PCR CT gene target data or underwent sequencing and hospitalisations that could be linked to these tests. METHODS: To calculate the instantaneous growth rate for VOCs we have developed a generalised additive model fit to multiple splines and varying day of the week effects. We have further modelled the instantaneous reproduction number Rt for the B.1.1.7 and B.1.617.2 variants and included a doubly interval censored model to temporally adjust the confirmed variant cases. RESULTS: We observed a clear replacement of the predominant B.1.1.7 by the B.1.617.2 variant without observing sustained exponential growth in other novel variants. Modelled exponential growth of RT PCR gene target triple-positive cases was initially detected in the youngest age groups, although we now observe across all ages a very small doubling time of 10.7 (95% CI 9.1 to 13.2) days and 8 (95% CI 6.9 to 9.1) days for cases and hospitalisations, respectively. We observe that growth in RT PCR gene target triple-positive cases was first detected in the Indian ethnicity group in late February, with a peak of 0.06 (95% CI 0.07 to 0.05) in the instantaneous growth rate, but is now maintained by the white ethnicity groups, observing a doubling time of 6.8 (95% CI 4.9 to 11) days. Rt analysis indicates a reproduction number advantage of 0.45 for B.1.617.2 relative to B.1.1.7, with the Rt value peaking at 1.85 for B.1.617.2. CONCLUSIONS: Our results illustrate a clear transmission advantage for the B.1.617.2 variant and the growth in hospitalisations illustrates that this variant is able to maintain exponential growth within age groups that are largely doubly vaccinated. There are concerning signs of intermittent growth in the B.1.351 variant, reaching a 28-day doubling time peak in March 2021, although this variant is presently not showing any evidence of a transmission advantage over B.1.617.2. Step 1b of the UK national lockdown easing was sufficient to precipitate exponential growth in B.1.617.2 cases for most regions and younger adult age groups. The final stages of NPI easing appeared to have a negligible impact on the growth of B.1.617.2 with every region experiencing sustained exponential growth from step 2. Nonetheless, early targeted local NPIs appeared to markedly reduced growth of B.1.617.2. Later localised interventions, at a time of higher prevalence and greater geographic dispersion of this variant, appeared to have a negligible impact on growth.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34819293
DOI: 10.1136/bmjopen-2021-056636

95. Weiss A, Touret F, Baronti C, et al. Niclosamide shows strong antiviral activity in a human airway model of SARS-CoV-2 infection and a conserved potency against the Alpha (B.1.1.7), Beta (B.1.351) and Delta variant (B.1.617.2). PLoS One. 2021;16(12):e0260958. DOI: 10.1371/journal.pone.0260958
ABSTRACT: SARS-CoV-2 variants are emerging with potential increased transmissibility highlighting the great unmet medical need for new therapies. Niclosamide is a potent anti-SARS-CoV-2 agent that has advanced in clinical development. We validate the potent antiviral efficacy of niclosamide in a SARS-CoV-2 human airway model. Furthermore, niclosamide remains its potency against the D614G, Alpha (B.1.1.7), Beta (B.1.351), and Delta (B.1.617.2) variants. Our data further support the potent anti-SARS-CoV-2 properties of niclosamide and highlights its great potential as a therapeutic agent for COVID-19.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34855904

DOI: 10.1371/journal.pone.0260958

96. Wurtzer S, Waldman P, Levert M, et al. SARS-CoV-2 genome quantification in wastewaters at regional and city scale allows precise monitoring of the whole outbreaks dynamics and variants spreading in the population. Sci Total Environ. 2021:152213. DOI: 10.1016/j.scitotenv.2021.152213
ABSTRACT: SARS-CoV-2 is a coronavirus causing a globalized outbreak called COVID-19. SARS-CoV-2 transmission is associated with inhalation of contaminated respiratory droplets and could causes severe complications. Until today several "waves" of infections have been observed despite implementation of strict health policies. Decisions for such sanitary measures are based on population health monitoring. Unfortunately, for COVID-19, a significant proportion of individuals are asymptomatic but play a role in the virus transmission. To overcome these limitations, several strategies were developed including genome quantification in wastewater that could allow monitoring of the health status of population, since shedding of SARS-CoV-2 in patient stool is frequent. Wastewater-based epidemiology (WBE) was established and several countries implemented this approach to allow COVID-19 outbreak monitoring. In France, the OBEPINE project performed a quantitative analysis of SARS-CoV-2 in raw wastewater samples collected from major wastewater treatment plants (WWTP) since March 2020. In the greater Paris area 1101 samples (507 for five WWTP and 594 for sewer) were collected. This 16months monitoring allows us to observe the outbreak dynamics. Comparison of WBE indicators with health data lead to several important observation; the good level of correlation with incidence rates, the average 3days lead time, and the sensitivity (WBE change when incidence is > to 7/100000 inhabitants). We also compared the local monitoring (city level) with the regional monitoring, to help cluster identification. Moreover, variants of concern (VOC) emerged due to the selection pressure. We developed a specific RT-qPCR method targeting the deletion H69-V70 in the spike protein, using this deletion as a proxy of the B.1.1.7 presence in the wastewater. With this data we demonstrate the predominant role played by this strain in the third wave. All these results allow a better description and understanding of the pandemic and highlight the role of such WBE indicators.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34896511
DOI: 10.1016/j.scitotenv.2021.152213

97. Yakovleva A, Kovalenko G, Redlinger M, et al. Tracking SARS-COV-2 Variants Using Nanopore Sequencing in Ukraine in Summer 2021. Res Sq. 2021. DOI: 10.21203/rs.3.rs-1044446/v1
ABSTRACT: Since spring 2020, Ukraine has experienced at least two COVID-19 waves and has just entered a third wave in autumn 2021. The use of real-time genomic epidemiology has enabled the tracking of SARS-CoV-2 circulation patterns worldwide, thus informing evidence-based public health decision making, including implementation of travel restrictions and vaccine rollout strategies. However, insufficient capacity for local genetic sequencing in Ukraine and other Lower and Middle-Income countries limit opportunities for similar analyses. Herein, we report local sequencing of 24 SARS-CoV-2 genomes from patient samples collected in Kyiv in July 2021 using Oxford Nanopore MinION technology. Together with other published Ukrainian SARS-COV-2 genomes sequenced mostly abroad, our data suggest that the second wave of the epidemic in Ukraine (February-April 2021) was dominated by the Alpha variant of concern (VOC), while the beginning of the third wave has been dominated by the Delta VOC. Furthermore, our phylogeographic analysis revealed that the Delta variant was introduced into Ukraine in summer 2021 from multiple locations worldwide, with most introductions coming from Central and Eastern European countries. This study highlights the need to urgently integrate affordable and easily-scaled pathogen sequencing technologies in locations with less developed genomic infrastructure, in order to support local public health decision making.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34873595
DOI: 10.21203/rs.3.rs-1044446/v1

98. Yeboah P, Daliri DB, Abdin AY, et al. Knowledge into the Practice against COVID-19: A Cross-Sectional Study from Ghana. International Journal of Environmental Research and Public Health. 2021;18(24):12902. DOI: 10.3390/ijerph182412902
ABSTRACT: The COVID-19 pandemic has affected populations globally, including Ghana. Knowledge of the COVID-19 disease, and the application of preventive public health interventions are pivotal to its control. Besides a lockdown, measures taken against the spread of the virus include the wearing of face masks, social distancing, regular hand washing with soap and, more recently, vaccination against the virus. In order to establish a possible

link between the knowledge of the disease and compliance with preventive measures, including vaccination, a cross-sectional study employing an interview-structured questionnaire was conducted in six regions of Ghana (n = 1560). An adequate level of knowledge of COVID-19 (69.9%) was reported. The linear multiple regression analysis fur-ther explicated the differences in the knowledge of COVID-19 among the respondents by their knowledge of cholera and influenza (adjusted R-Square = 0.643). Despite this profound knowledge of the illness, two thirds of the respondents were unwilling to follow basic preventive measures and only 35.3% were willing to be vaccinated. Amazingly, neither knowledge of COVID-19 nor the so-cio-demographic characteristics had any meaningful influence on the practice of preventive measures. Personal attitude leading to efficient public compliance with preventive measures, there-fore, is a critical issue demanding special attention and effective interventions by the government and locals with authority to curb the spread of the pandemic which surpasses the traditional channels of public health communication. This includes a roll-out of persuasion, possibly including public figures and influencers, and in any case, a balanced and open discussion addressing the acceptance of the COVID-19 vaccine in order to avoid new variants and comparable problems currently facing many countries of Western Europe. Indeed, a profound hesitancy against vaccination may turn African countries such as Ghana for many years into hotspots of new viral variants.
URL: https://www.mdpi.com/1660-4601/18/24/12902/pdf
DOI: 10.3390/ijerph182412902

99. Yuan B, Zhanwei D, Mingda X, et al. International risk of SARS-CoV-2 Omicron variant importations originating in South Africa. 2021.
ABSTRACT: Omicron, a fast-spreading SARS-CoV-2 variant of concern reported to the World Health Organization on November 24, 2021, has raised international alarm. We estimated there is at least 50% chance that Omicron had been introduced by travelers from South Africa into all of the 30 countries studied by November 27, 2021.
URL: https://medrxiv.org/cgi/content/short/2021.12.07.21267410

100. Yunlong Richard C, Jing W, Fanchong J, et al. B.1.1.529 escapes the majority of SARS-CoV-2 neutralizing antibodies of diverse epitopes. 2021.
ABSTRACT: The SARS-CoV-2 B.1.1.529 variant (Omicron) contains 15 mutations on the receptor-binding domain (RBD). How Omicron would evade RBD neutralizing antibodies (NAbs) and humoral immunity requires immediate investigation. Here, we used high-throughput yeast display screening1,2 to determine the RBD escaping mutation profiles for 247 human anti-RBD NAbs identified from SARS-CoV/SARS-CoV-2 convalescents and vaccinees. Based on the results, NAbs could be unsupervised clustered into six epitope groups (A-F), which is highly concordant with knowledge-based structural classifications3-5. Strikingly, various single mutations of Omicron could impair NAbs of different epitope groups. Specifically, NAbs in Group A-D, whose epitope overlaps with ACE2-binding motif, are largely escaped by K417N, N440K, G446S, E484A, Q493K, and G496S. Group E (S309 site)6 and F (CR3022 site)7 NAbs, which often exhibit broad sarbecovirus neutralizing activity, are less affected by Omicron, but still, a subset of NAbs are escaped by G339D, S371L, and S375F. Furthermore, B.1.1.529 pseudovirus neutralization and RBD binding assay showed that single mutation tolerating NAbs could also be escaped due to multiple synergetic mutations on their epitopes. In total, over 85% of the tested NAbs are escaped by Omicron. Regarding NAb drugs, LY-CoV016/LY-CoV555 cocktail, REGN-CoV2 cocktail, AZD1061/AZD8895 cocktail, and BRII-196 were escaped by Omicron, while VIR7831 and DXP-604 still function at reduced efficacy. Together, data suggest Omicron could cause significant humoral immune evasion, while NAbs targeting the sarbecovirus conserved region remain most effective. Our results offer instructions for developing NAb drugs and vaccines against Omicron and future variants.
URL: https://biorxiv.org/cgi/content/short/2021.12.07.470392

101. Zhang L, Li Q, Liang Z, et al. The significant immune escape of pseudotyped SARS-CoV-2 Variant Omicron. Emerg Microbes Infect. 2021:1-11. DOI: 10.1080/22221751.2021.2017757
ABSTRACT: SummaryThe emergence of Omicron has brought new challenges to fight against SARS-CoV-2. A large number of mutations in the Spike protein suggest that its susceptibility to immune protection elicited by the existing COVID-19 infection and vaccines may be altered. In this study, we constructed the pseudotyped SARS-CoV-2 variant Omicron. The sensitivity of 28 serum samples from COVID-19 convalescent patients infected with SARS-CoV-2 original strain was tested against pseudotyped Omicron as well as the other viruses of concern (VOCs, Alpha,

Beta, Gamma, Delta) and viruses of interest (VOIs, Lambda, Mu). Our results indicated that the mean neutralization ED50 of these sera against Omicron decreased to 66which is about 8.4 folds compared to the D614G reference strain (ED50 = 556), whereas the neutralization activity of other VOC and VOI pseudotyped viruses decreased only about 1.2-4.5 folds. The finding from our in vitro assay suggest that Omicron variant may lead to more significant escape from immune protection elicited by previous SARS-CoV-2 infection and perhaps even by existing COVID-19 vaccines.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34890524
DOI: 10.1080/22221751.2021.2017757

102. Zhao S, Lou J, Cao L, et al. Differences in the case fatality risks associated with SARS-CoV-2 Delta and non-Delta variants in relation to vaccine coverage: An early ecological study in the United Kingdom. Infect Genet Evol. 2021;97:105162. DOI: 10.1016/j.meegid.2021.105162
ABSTRACT: The circulation of SARS-CoV-2 Delta (i.e., B.1.617.2) variants challenges the pandemic control. Our analysis showed that in the United Kingdom (UK), the reported case fatality ratio (CFR) decreased from May to July 2021 for non-Delta variant, whereas the decreasing trends of the CFR of Delta variant appeared weak and insignificant. The association between vaccine coverage and CFR might be stratified by different circulating variants. Due to the limitation of ecological study design, the interpretation of our results should be treated with caution.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34843993
DOI: 10.1016/j.meegid.2021.105162

Appendix 1: Evidence Search Details

Filters, Limits & Exclusions:	English only December 3, 2021 – December 17, 2021
Sources Searched:	• Agency for Clinical Innovation and New South Wales Government • CanCOVID • CBC • CDC • Center for Infectious Disease Research and Policy (CIDRAP) • COVID-19 Best Evidence Front Door, University of Michigan • COVID-19 Immunity Task Force • COVID-END • Embase • European Centres for Disease Prevention and Control (ECDC) • Google • Library and Knowledge Services (NHS, England) • McMaster Plus • Medline • National Collaborating Centre for Infectious Diseases • National Collaborating Centre for Methods and Tools • National Health Library & Knowledge Service (Ireland) • Newfoundland and Labrador Centre for Applied Health Research • Ontario Science Table • Prevent Epidemics • Public Health England • Public Health Ontario • Strategy for Patient-Orient Research (SPOR) Evidence Alliance • Usher Network for COVID-19 Evidence Reviews (UNCOVER), Usher Institute, University of Edinburgh Veterans Affairs Evidence Synthesis Program
Librarian(s):	Lukas Miller, Clinical Librarian, Saskatchewan Health Authority Brianna Howell-Spooner, Clinical Librarian, Saskatchewan Health Authority

Appendix 2: Search Strategies

Ovid MEDLINE(R) ALL <1946 to December 16, 2021>

#	Searches	Results
1	(coronavirus/ or betacoronavirus/ or coronavirus infections/) and (disease outbreaks/ or epidemics/ or pandemics/)	40095
2	(nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARSCOV2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kf.	199183
3	((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kf.	59356
4	((coronavirus* or corona virus* or betacoronavirus* or COVID*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kf.	83056
5	(longCOVID* or postCOVID* or postcoronavirus* or postSARS*).ti,ab,kf.	24
6	or/1-5	206169
7	("variant of concern" or "variants of concern").tw,kf.	957
8	SARS-CoV-2 variants.ox. [mesh supplementary concept]	118
9	(((variant? or mutation? or strain? or lineage?) adj3 virus*) or ((variant? or mutation? or strain? or lineage?) adj3 viral)).ti,kf. or (((variant? or mutation? or strain? or lineage?) adj3 virus*) or ((variant? or mutation? or strain? or lineage?) adj3 viral)).ab. /freq=2	14679
10	((new or newer or newest or novel) adj2 variant?).ti,kf. or ((new or newer or newest or novel) adj2 variant?).ab. /freq=2	7330
11	("20I/S:501Y.V1" or "20I/501Y.V1" or "B.1.1.7" or "B117" or "501YV1" or "GR/501Y.V1" or "GRY" or (alpha adj3 variant?)).ti,kf. or ("20I/S:501Y.V1" or "20I/501Y.V1" or "B.1.1.7" or "B117" or "501YV1" or "GR/501Y.V1" or "GRY" or (alpha adj3 variant?)).ab. /freq=2 [WHO Alpha]	1725
12	("B.1.351" or "B1351" or "20H/501Y.V2" or "GH/501Y.V2" or "20H/S:501Y.V2" or "501YV2" or (beta adj3 variant?)).ti,kf. or ("B.1.351" or "B1351" or "20H/501Y.V2" or "GH/501Y.V2" or "20H/S:501Y.V2" or "501YV2" or (beta adj3 variant?)).ab. /freq=2 [WHO Beta]	1294
13	("P.1" or "P1" or "20J/501Y.V3" or "501YV3" or "GR/501Y.V3" or "20J/S:501Y.V3" or (gamma adj3 variant?)).ti,kf. or ("P.1" or "P1" or "20J/501Y.V3" or "501YV3" or "GR/501Y.V3" or "20J/S:501Y.V3" or (gamma adj3 variant?)).ab. /freq=2 [WHO Gamma]	16355
14	("B.1.617.2" or "B16172" or "G/452R.V3" or "G/452RV3" or "G452RV3" or "G452R.V3" or "21A/S:478K" or (delta adj3 variant?)).ti,kf. or ("B.1.617.2" or "B16172" or "G/452R.V3" or "G/452RV3" or "G452RV3" or "G452R.V3" or "21A/S:478K" or (delta adj3 variant?)).ab. /freq=2 [WHO Delta]	525
15	("B.1.1.529" or "B11529" or "GR/484A" or (omicron adj3 variant?)).ti,kf. [WHO Omicron]	26
16	or/7-15	41735
17	exp *Epidemiology/ or exp *Morbidity/ or exp *Mortality/	90922

18	(epidemiolog* or morbidit* or mortalit* or "cause of death" or causation or etiolog* or disease outcome? or fatal outcome? or survival or incidence? or prevalence? or attack rate or basic reproduction or "R0" or "R 0" or transmissibility).tw,kf.	3779359
19	17 or 18	3795108
20	6 and 16 and 19	681
21	limit 20 to (english language and yr="2021 -Current")	634
22	limit 21 to dt=20211203-20211217	39

Embase <1974 to 2021 December 16>

#	Searches	Results
1	sars-related coronavirus/	482
2	(coronavirinae/ or betacoronavirus/ or coronavirus infection/) and (epidemic/ or pandemic/)	10675
3	(nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARS-COV2 or SARSCOV2 or SARS coronavirus 2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kw,hw,ot.	202887
4	((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kw,hw,ot.	180960
5	(longCOVID* or postCOVID* or postcoronavirus* or postSARS*).ti,ab,kw,hw,ot.	56
6	((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kw,ot.	12237
7	((Wuhan or Hubei) adj5 pneumonia).ti,ab,kw,ot.	424
8	or/1-7	220763
9	("variant of concern" or "variants of concern").tw,ot,kf.	739
10	(((variant? or mutation? or strain? or lineage?) adj3 virus*) or ((variant? or mutation? or strain? or lineage?) adj3 viral)).ti,kf. or (((variant? or mutation? or strain? or lineage?) adj3 virus*) or ((variant? or mutation? or strain? or lineage?) adj3 viral)).ab. /freq=2	14266
11	((new or newer or newest or novel) adj2 variant?).ti,kf. or ((new or newer or newest or novel) adj2 variant?).ab. /freq=2	9226
12	("20I/S:501Y.V1" or "20I/501Y.V1" or "B.1.1.7" or "B117" or "501YV1" or "GR/501Y.V1" or "GRY" or (alpha adj2 variant?)).ti,kf. or ("20I/S:501Y.V1" or "20I/501Y.V1" or "B.1.1.7" or "B117" or "501YV1" or "GR/501Y.V1" or "GRY" or (alpha adj2 variant?)).ab. /freq=2 [WHO Alpha]	1094
13	("B.1.351" or "B1351" or "20H/501Y.V2" or "GH/501Y.V2" or "20H/S:501Y.V2" or "501YV2" or (beta adj2 variant?)).ti,kf. or ("B.1.351" or "B1351" or "20H/501Y.V2" or "GH/501Y.V2" or "20H/S:501Y.V2" or "501YV2" or (beta adj2 variant?)).ab. /freq=2 [WHO Beta]	873
14	("P.1" or "P1" or "20J/501Y.V3" or "501YV3" or "GR/501Y.V3" or "20J/S:501Y.V3" or (gamma adj2 variant?)).ti,kf. or ("P.1" or "P1" or "20J/501Y.V3" or "501YV3" or "GR/501Y.V3" or "20J/S:501Y.V3" or (gamma adj2 variant?)).ab. /freq=2 [WHO Gamma]	21514
15	("B.1.617.2" or "B16172" or "G/452R.V3" or "G/452RV3" or "G452RV3" or "G452R.V3" or "21A/S:478K" or (delta adj2 variant?)).ti,kf. or ("B.1.617.2" or "B16172" or "G/452R.V3" or "G/452RV3" or "G452RV3" or "G452R.V3" or "21A/S:478K" or (delta adj2 variant?)).ab. /freq=2 [WHO Delta]	345

16	("B.1.1.529" or "B11529" or "GR/484A" or (omicron adj3 variant?)).tw,kf. [WHO Omicron]	7
17	or/9-16	47204
18	exp *epidemiology/ or exp *mortality/ or exp *morbidity/	494752
19	(epidemiolog* or morbidit* or mortalit* or "cause of death" or causation or etiolog* or disease outcome? or fatal outcome? or survival or incidence? or prevalence? or attack rate or basic reproduction or "R0" or "R 0" or transmissibility).tw,kf.	5243891
20	18 or 19	5367070
21	8 and 17 and 20	529
22	limit 21 to (english language and yr="2021 -Current")	504
23	limit 22 to dd=20211203-20211217	36
24	limit 23 to medline	1
25	23 not 24	35

Other Sources

COVID AND [variant* OR delta OR alpha OR beta OR lambda OR mu OR gamma OR Omicron]