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## Archived Editions (COVID-19 Genomics and Precision Public Health Weekly Update)

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### COVID-19 Genomics and Precision Public Health Weekly Update Content

- Pathogen and Human Genomics Studies
- Non-Genomics Precision Health Studies
- News, Reviews and Commentaries

### Pathogen and Human Genomics Studies

- Containment of a multi-index B.1.1.7 outbreak on a university campus through a genomically-informed public health response (<https://www.medrxiv.org/content/10.1101/2022.01.04.22268758v1>)  
E Toth et al, MEDRXIV, January 5, 2022

The first cluster of SARS-CoV-2 cases with lineage B.1.1.7 in the state of Michigan was identified through intensive university-led surveillance sampling and targeted sequencing. A collaborative investigation and response was conducted by the local and state health departments, and the campus and athletic medicine COVID-19 response teams, using S-gene target failure screening and rapid genomic sequencing to inform containment strategies. A total of 50 cases of B.1.1.7-lineage SARS-CoV-2 were identified in this outbreak, which was due to three coincident introductions of B.1.1.7-lineage SARS-CoV-2, all of which were genetically distinct from lineages which later circulated in the broader community.

- Durability of Protection against COVID-19 Breakthrough Infections and Severe Disease by Vaccines in the United States (<https://www.medrxiv.org/content/10.1101/2022.01.05.22268648v1>)  
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Following primary vaccination, all three vaccines showed strong and durable protection against ICU admissions. Ad26.COV2.S showed a more durable level of protection against breakthrough infections and hospitalizations in line with published evidence of its durable antibody and cellular immune response, although its Vaccine Effectiveness (VE) at baseline after a single-dose is lower than that for the two-dose mRNA vaccines.

- Association between vaccination status and reported incidence of post-acute COVID-19 symptoms in Israel: a cross-sectional study of patients infected between March 2020 and November 2021 (<https://www.medrxiv.org/content/10.1101/2022.01.05.22268800v1>)  
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Vaccination with at least two doses of COVID-19 vaccine was associated with a substantial decrease in reporting the most common post-acute COVID19 symptoms. Our results suggest that, in addition to reducing the risk of acute illness, COVID-19 vaccination may have a protective effect against long COVID.

- Effectiveness of mRNA-1273 against SARS-CoV-2 omicron and delta variants (<https://www.medrxiv.org/content/10.1101/2022.01.07.22268919v1>)  
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The 2-dose VE against omicron infection was 30.4% (95% CI, 5.0%-49.0%) at 14-90 days after vaccination and declined quickly thereafter. The 3-dose VE was 95.2% (93.4%-96.4%) against delta infection and 62.5% (56.2%-67.9%) against omicron infection. The 3-dose VE against omicron infection was low among immunocompromised individuals (11.5%; 0.0%-66.5%). None of the cases (delta or omicron) vaccinated with 3 doses were hospitalized compared to 53 delta and 2 omicron unvaccinated cases.

- BNT162b2 post-exposure-prophylaxis against COVID-19 (<https://www.medrxiv.org/content/10.1101/2022.01.07.22268869v1>)  
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- Innate and adaptive immune defects associated with lower SARS-CoV-2 BNT162b2 mRNA vaccine response in elderly people (<https://www.medrxiv.org/content/10.1101/2022.01.07.22268806v1>)  
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Aging was associated with a lower anti-RBD IgG levels and a decreased magnitude and polyfunctionality of SARS-CoV-2 specific T cell response. The dramatic decrease in thymic function in the elderly, which fueled alteration in T cell homeostasis, and lower CD161+ T cell levels were associated with decreased T cell response two months after vaccination. Additionally, a deficient dendritic cell (DC) homing, activation and Toll like receptor (TLR)-mediated function, along with a

proinflammatory functional profile in monocytes, were observed in the elderly, which was also related to lower specific T cell response after vaccination.

- Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa (<https://www.nature.com/articles/d41586-021-03832-5?>)  
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In November 2021, genomic surveillance teams in South Africa and Botswana detected a new SARS-CoV-2 variant associated with a rapid resurgence of infections in Gauteng Province, South Africa. Within three days of the first genome being uploaded, it was designated a variant of concern (Omicron) by the World Health Organization and, within three weeks, had been identified in 87 countries. The Omicron variant is exceptional for carrying over 30 mutations in the spike glycoprotein, predicted to influence antibody neutralization and spike function.

- Association of genetic variations in ACE2, TIRAP and factor X with outcomes in COVID-19. (<https://pubmed.ncbi.nlm.nih.gov/34995294>)  
Traets Marissa J M et al. PloS one 2022 1 (1) e0260897

Between March and April 2020, 116 patients (35% female, median age 65 [inter quartile range 55-75] years) were included and treated according to the then applicable guidelines. Sixteen patients (14%) died, 44 patients (38%) had respiratory failure of whom 23 required endotracheal intubation for mechanical ventilation, and 20 patients (17%) developed venous thromboembolism. The percentage of TIRAP polymorphism carriers in the survivor group was 28% as compared to 0% in the non-survivor group ( $p = 0.01$ ).

- Association of a Third Dose of BNT162b2 Vaccine With Incidence of SARS-CoV-2 Infection Among Health Care Workers in Israel (<https://jamanetwork.com/journals/jama/fullarticle/2788104>)  
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In this cohort study of 1928 health care workers in Israel who were previously vaccinated with a 2-dose series of BNT162b2, administration of a booster dose compared with not receiving one was significantly associated with lower risk of SARS-CoV-2 infection during a median of 39 days of follow-up (adjusted hazard ratio, 0.07). Meaning Among health care workers previously vaccinated with a 2-dose series of BNT162b2, administration of a booster dose compared with not receiving one was significantly associated with a lower rate of SARS-CoV-2 infection in short-term follow-up.

- Clinical outcomes among patients infected with Omicron (B.1.1.529) SARS-CoV-2 variant in southern California (<https://www.medrxiv.org/content/10.1101/2022.01.11.22269045v1>)  
JA Lewnard et al, MEDRXIV, January 11, 2022

Our analyses included 52,297 cases with SGTF (Omicron) and 16,982 cases with non-SGTF (Delta [B.1.617.2]) infections, respectively. Hospital admissions occurred among 235 (0.5%) and 222 (1.3%) of cases with Omicron and Delta variant infections, respectively. Among cases first tested in outpatient settings, the adjusted hazard ratios for any subsequent hospital admission and symptomatic hospital

admission associated with Omicron variant infection were 0.48 (0.36-0.64) and 0.47 (0.35-0.62), respectively. Rates of ICU admission and mortality after an outpatient positive test were 0.26 (0.10-0.73) and 0.09 (0.01-0.75) fold as high among cases with Omicron variant infection as compared to cases with Delta variant infection. Zero cases with Omicron variant infection received mechanical ventilation, as compared to 11 cases with Delta variant infections

- Clinical validation of engineered CRISPR/Cas12a for rapid SARS-CoV-2 detection (<https://www.nature.com/articles/s43856-021-00066-4>)  
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- Infectious viral load in unvaccinated and vaccinated patients infected with SARS-CoV-2 WT, Delta and Omicron (<https://www.medrxiv.org/content/10.1101/2022.01.10.22269010v1>)  
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Quantitative infectious viral titers (IVTs) can give detailed insights into virus shedding kinetics. Vaccination was associated with lower infectious titers and faster clearance for Delta, showing that vaccination would also lower transmission risk. Omicron vaccine breakthrough infections did not show elevated IVTs compared to Delta, suggesting that other mechanisms than increase viral load contribute to the high infectiousness of Omicron

- Effectiveness of BNT162b2 Vaccine against Critical Covid-19 in Adolescents. (<https://pubmed.ncbi.nlm.nih.gov/35021004>)  
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A total of 445 case patients and 777 controls were enrolled. Overall, 17 case patients (4%) and 282 controls (36%) had been fully vaccinated. Of the case patients, 180 (40%) were admitted to the ICU, and 127 (29%) required life support; only 2 patients in the ICU had been fully vaccinated. The overall effectiveness of the BNT162b2 vaccine against hospitalization for Covid-19 was 94% (95% confidence interval [CI], 90 to 96); the effectiveness was 95% (95% CI, 91 to 97) among test-negative controls and 94% (95% CI, 89 to 96) among syndrome-negative controls. The effectiveness was 98% against ICU admission and 98% against Covid-19 resulting in the receipt of life support. All 7 deaths occurred in patients who were unvaccinated.

- Duration of Protection against Mild and Severe Disease by Covid-19 Vaccines. (<https://pubmed.ncbi.nlm.nih.gov/35021002>)  
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Vaccine effectiveness against symptomatic Covid-19 with the delta variant peaked in the early weeks after receipt of the second dose and then decreased by 20 weeks to 44.3% (95% confidence interval [CI], 43.2 to 45.4) with the ChAdOx1-S vaccine and to 66.3% (95% CI, 65.7 to 66.9) with the BNT162b2 vaccine. Waning of vaccine effectiveness was greater in persons 65 years of age or older than in those 40 to 64 years of age. At 20 weeks or more after vaccination, vaccine effectiveness decreased less against both hospitalization, to 80.0% (95% CI, 76.8 to 82.7) with the ChAdOx1-S

vaccine and 91.7% (95% CI, 90.2 to 93.0) with the BNT162b2 vaccine, and death, to 84.8% (95% CI, 76.2 to 90.3) and 91.9% (95% CI, 88.5 to 94.3), respectively.

- Effectiveness of Covid-19 Vaccines over a 9-Month Period in North Carolina.

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For the two-dose regimens of messenger RNA (mRNA) vaccines BNT162b2 (30 µg per dose) and mRNA-1273 (100 µg per dose), vaccine effectiveness against Covid-19 was 94.5% (95% confidence interval [CI], 94.1 to 94.9) and 95.9% (95% CI, 95.5 to 96.2), respectively, at 2 months after the first dose and decreased to 66.6% (95% CI, 65.2 to 67.8) and 80.3% (95% CI, 79.3 to 81.2), respectively, at 7 months. Among early recipients of BNT162b2 and mRNA-1273, effectiveness decreased by approximately 15 and 10 percentage points, respectively, from mid-June to mid-July, when the delta variant became dominant.

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We included 5,144 patients from wave four and 11,609 from prior waves. Risk of all outcomes was lower in wave four compared to the Delta-driven wave three (adjusted Hazard Ratio (aHR) [95% confidence interval (CI)] for death 0.27 [0.19; 0.38]. Risk reduction was lower when adjusting for vaccination and prior diagnosed infection (aHR:0.41, 95% CI: 0.29; 0.59) and reduced further when accounting for unascertained prior infections (aHR: 0.72). Vaccine protection was maintained in wave four (aHR for outcome of death: 0.24; 95% CI: 0.10; 0.58).

## Non-Genomics Precision Health Studies

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- Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa (<https://www.nature.com/articles/d41586-021-03832-5?>)  
R Viana et al, Nature, January 7, 2022

In November 2021, genomic surveillance teams in South Africa and Botswana detected a new SARS-CoV-2 variant associated with a rapid resurgence of infections in Gauteng Province, South Africa. Within three days of the first genome being uploaded, it was designated a variant of concern (Omicron) by the World Health Organization and, within three weeks, had been identified in 87 countries. The Omicron variant is exceptional for carrying over 30 mutations in the spike glycoprotein, predicted to influence antibody neutralization and spike function.

- Association of genetic variations in ACE2, TIRAP and factor X with outcomes in COVID-19. (<https://pubmed.ncbi.nlm.nih.gov/34995294>)  
Traets Marissa J M et al. PloS one 2022 1 (1) e0260897

Between March and April 2020, 116 patients (35% female, median age 65 [inter quartile range 55-75] years) were included and treated according to the then applicable guidelines. Sixteen patients (14%) died, 44 patients (38%) had respiratory failure of whom 23 required endotracheal intubation for mechanical ventilation, and 20 patients (17%) developed venous thromboembolism. The percentage of TIRAP polymorphism carriers in the survivor group was 28% as compared to 0% in the non-survivor group ( $p = 0.01$ ).

- Association of a Third Dose of BNT162b2 Vaccine With Incidence of SARS-CoV-2 Infection Among Health Care Workers in Israel (<https://jamanetwork.com/journals/jama/fullarticle/2788104>)

A Spitzer et al, JAMA< January 10, 2022

In this cohort study of 1928 health care workers in Israel who were previously vaccinated with a 2-dose series of BNT162b2, administration of a booster dose compared with not receiving one was significantly associated with lower risk of SARS-CoV-2 infection during a median of 39 days of follow-up (adjusted hazard ratio, 0.07). Meaning Among health care workers previously vaccinated with a 2-dose series of BNT162b2, administration of a booster dose compared with not receiving one was significantly associated with a lower rate of SARS-CoV-2 infection in short-term follow-up.

- Clinical outcomes among patients infected with Omicron (B.1.1.529) SARS-CoV-2 variant in southern California (<https://www.medrxiv.org/content/10.1101/2022.01.11.22269045v1>)

JA Lewnard et al, MEDRXIV, January 11, 2022

Our analyses included 52,297 cases with SGTF (Omicron) and 16,982 cases with non-SGTF (Delta [B.1.617.2]) infections, respectively. Hospital admissions occurred among 235 (0.5%) and 222 (1.3%) of cases with Omicron and Delta variant infections, respectively. Among cases first tested in outpatient settings, the adjusted hazard ratios for any subsequent hospital admission and symptomatic hospital admission associated with Omicron variant infection were 0.48 (0.36-0.64) and 0.47 (0.35-0.62), respectively. Rates of ICU admission and mortality after an outpatient positive test were 0.26 (0.10-0.73) and 0.09 (0.01-0.75) fold as high among cases with Omicron variant infection as compared to cases with Delta variant infection. Zero cases with Omicron variant infection received mechanical ventilation, as compared to 11 cases with Delta variant infections

- Clinical validation of engineered CRISPR/Cas12a for rapid SARS-CoV-2 detection (<https://www.nature.com/articles/s43856-021-00066-4>)

LT Nguyen et al, Communications Medicine, January 12, 2022

- Infectious viral load in unvaccinated and vaccinated patients infected with SARS-CoV-2 WT, Delta and Omicron (<https://www.medrxiv.org/content/10.1101/2022.01.10.22269010v1>)

O Puhash et al, MEDRXIV, January 11, 2022

Quantitative infectious viral titers (IVTs) can give detailed insights into virus shedding kinetics. Vaccination was associated with lower infectious titers and faster clearance for Delta, showing that vaccination would also lower transmission risk. Omicron vaccine breakthrough infections did not show

elevated IVTs compared to Delta, suggesting that other mechanisms than increase viral load contribute to the high infectiousness of Omicron

- Effectiveness of BNT162b2 Vaccine against Critical Covid-19 in Adolescents.

(<https://pubmed.ncbi.nlm.nih.gov/35021004>)

Olson Samantha M et al. The New England journal of medicine 2022 1

A total of 445 case patients and 777 controls were enrolled. Overall, 17 case patients (4%) and 282 controls (36%) had been fully vaccinated. Of the case patients, 180 (40%) were admitted to the ICU, and 127 (29%) required life support; only 2 patients in the ICU had been fully vaccinated. The overall effectiveness of the BNT162b2 vaccine against hospitalization for Covid-19 was 94% (95% confidence interval [CI], 90 to 96); the effectiveness was 95% (95% CI, 91 to 97) among test-negative controls and 94% (95% CI, 89 to 96) among syndrome-negative controls. The effectiveness was 98% against ICU admission and 98% against Covid-19 resulting in the receipt of life support. All 7 deaths occurred in patients who were unvaccinated.

- Duration of Protection against Mild and Severe Disease by Covid-19 Vaccines.

(<https://pubmed.ncbi.nlm.nih.gov/35021002>)

Andrews Nick et al. The New England journal of medicine 2022 1

Vaccine effectiveness against symptomatic Covid-19 with the delta variant peaked in the early weeks after receipt of the second dose and then decreased by 20 weeks to 44.3% (95% confidence interval [CI], 43.2 to 45.4) with the ChAdOx1-S vaccine and to 66.3% (95% CI, 65.7 to 66.9) with the BNT162b2 vaccine. Waning of vaccine effectiveness was greater in persons 65 years of age or older than in those 40 to 64 years of age. At 20 weeks or more after vaccination, vaccine effectiveness decreased less against both hospitalization, to 80.0% (95% CI, 76.8 to 82.7) with the ChAdOx1-S vaccine and 91.7% (95% CI, 90.2 to 93.0) with the BNT162b2 vaccine, and death, to 84.8% (95% CI, 76.2 to 90.3) and 91.9% (95% CI, 88.5 to 94.3), respectively.

- Effectiveness of Covid-19 Vaccines over a 9-Month Period in North Carolina.

(<https://pubmed.ncbi.nlm.nih.gov/35020982>)

Lin Dan-Yu et al. The New England journal of medicine 2022 1

For the two-dose regimens of messenger RNA (mRNA) vaccines BNT162b2 (30 µg per dose) and mRNA-1273 (100 µg per dose), vaccine effectiveness against Covid-19 was 94.5% (95% confidence interval [CI], 94.1 to 94.9) and 95.9% (95% CI, 95.5 to 96.2), respectively, at 2 months after the first dose and decreased to 66.6% (95% CI, 65.2 to 67.8) and 80.3% (95% CI, 79.3 to 81.2), respectively, at 7 months. Among early recipients of BNT162b2 and mRNA-1273, effectiveness decreased by approximately 15 and 10 percentage points, respectively, from mid-June to mid-July, when the delta variant became dominant.

- Rapid and Accurate Identification of SARS-CoV-2 Omicron Variants Using Droplet Digital PCR (RT-ddPCR) (<https://www.medrxiv.org/content/10.1101/2022.01.11.22268981v1>)

R Mills et al, January 12, 2022

- Outcomes of laboratory-confirmed SARS-CoV-2 infection in the Omicron-driven fourth wave compared with previous waves in the Western Cape Province, South Africa (<https://www.medrxiv.org/content/10.1101/2022.01.12.22269148v1>)  
MA Davies et al, MEDRXIV, January 12, 2022

We included 5,144 patients from wave four and 11,609 from prior waves. Risk of all outcomes was lower in wave four compared to the Delta-driven wave three (adjusted Hazard Ratio (aHR) [95% confidence interval (CI)] for death 0.27 [0.19; 0.38]. Risk reduction was lower when adjusting for vaccination and prior diagnosed infection (aHR:0.41, 95% CI: 0.29; 0.59) and reduced further when accounting for unascertained prior infections (aHR: 0.72). Vaccine protection was maintained in wave four (aHR for outcome of death: 0.24; 95% CI: 0.10; 0.58).

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