

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

- Initial analysis of viral dynamics and circulating viral variants during the mRNA-1273 Phase 3 COVE trial (<https://www.nature.com/articles/s41591-022-01679-5>)
R Pajon et al, Nature Medicine, February 10, 2022

We assessed the impact of mRNA-1273 vaccination in the ongoing COVE trial (number NCT04470427) on SARS-CoV-2 copy number and shedding, burden of disease and infection, and viral variants. While additional study is needed, our data show that in SARS-CoV-2-infected individuals, vaccination reduced both the viral copy number and duration of detectable viral RNA, which may be markers for the risk of virus transmission.

- Genomic Surveillance for SARS-CoV-2 Variants: Predominance of the Delta (B.1.617.2) and Omicron (B.1.1.529) Variants – United States, June 2021–January 2022
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CDC's SARS-CoV-2 genomic surveillance has been expanded to incorporate sequence data from public repositories and to produce weighted estimates of variant proportions at the jurisdiction level. The Delta (B.1.617.2 and AY sublineages) variant rose to predominance in late June 2021, followed by the rapid rise of Omicron (B.1.1.529 and BA sublineages) in December 2021. The dynamic landscape of SARS-CoV-2 variants in 2021, including Delta- and Omicron-driven resurgences of SARS-CoV-2 transmission across the United States, underscores the importance of robust genomic surveillance efforts to inform public health planning and practice.

- Model-based estimates of deaths averted and cost per life saved by scaling-up mRNA COVID-19 vaccination in low and lower-middle income countries in the COVID-19 Omicron variant era (<https://www.medrxiv.org/content/10.1101/2022.02.08.22270465v1>)
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Scaling up vaccination to provide three doses of mRNA vaccine to everyone in LIC/LMIC would cost \$61.2 billion and avert 1.5 million deaths from COVID-19 at a cost of \$40,800 per death averted. Lower estimated infection fatality ratios, higher cost-per-dose, and lower vaccine effectiveness or uptake lead to higher cost-per-death averted estimates in the analysis. Interpretation: Scaling up COVID-19 global vaccination would avert millions of COVID-19 deaths and represents a reasonable investment in the context of the value of a statistical life (VSL). Given the magnitude of expected mortality facing LIC/LMIC without vaccination, this effort should be an urgent priority.

- Monitoring SARS-CoV-2 in wastewater during New York City's second wave of COVID-19: Sewershed-level trends and relationships to publicly available clinical testing data (<https://www.medrxiv.org/content/10.1101/2022.02.08.22270666v1>)
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Researchers say that the new variant is probably driving the surge because it is able to evade the body's immune defenses.

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Thus, our data indicates that mRNA vaccination may generate more neutralizing RBD antibodies than natural immunity. It further suggests a potential need to maintain high RBD antibody levels to control the more infectious SARS-CoV-2 variants.

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(<https://www.nature.com/articles/s41591-022-01679-5>)

R Pajon et al, Nature Medicine, February 10, 2022

We assessed the impact of mRNA-1273 vaccination in the ongoing COVE trial (number NCT04470427) on SARS-CoV-2 copy number and shedding, burden of disease and infection, and viral variants. While additional study is needed, our data show that in SARS-CoV-2-infected individuals,

vaccination reduced both the viral copy number and duration of detectable viral RNA, which may be markers for the risk of virus transmission.

- Genomic Surveillance for SARS-CoV-2 Variants: Predominance of the Delta (B.1.617.2) and Omicron (B.1.1.529) Variants – United States, June 2021–January 2022
(https://www.cdc.gov/mmwr/volumes/71/wr/mm7106a4.htm?s_cid=mm7106a4_x)
AS Lambrou et al, MMWR, February 10, 2022

CDC's SARS-CoV-2 genomic surveillance has been expanded to incorporate sequence data from public repositories and to produce weighted estimates of variant proportions at the jurisdiction level. The Delta (B.1.617.2 and AY sublineages) variant rose to predominance in late June 2021, followed by the rapid rise of Omicron (B.1.1.529 and BA sublineages) in December 2021. The dynamic landscape of SARS-CoV-2 variants in 2021, including Delta- and Omicron-driven resurgences of SARS-CoV-2 transmission across the United States, underscores the importance of robust genomic surveillance efforts to inform public health planning and practice.

- Model-based estimates of deaths averted and cost per life saved by scaling-up mRNA COVID-19 vaccination in low and lower-middle income countries in the COVID-19 Omicron variant era
(<https://www.medrxiv.org/content/10.1101/2022.02.08.22270465v1>)

A Savinkina et al, MEDRXIV, February 9, 2022

Scaling up vaccination to provide three doses of mRNA vaccine to everyone in LIC/LMIC would cost \$61.2 billion and avert 1.5 million deaths from COVID-19 at a cost of \$40,800 per death averted. Lower estimated infection fatality ratios, higher cost-per-dose, and lower vaccine effectiveness or uptake lead to higher cost-per-death averted estimates in the analysis. Interpretation: Scaling up COVID-19 global vaccination would avert millions of COVID-19 deaths and represents a reasonable investment in the context of the value of a statistical life (VSL). Given the magnitude of expected mortality facing LIC/LMIC without vaccination, this effort should be an urgent priority.

- Monitoring SARS-CoV-2 in wastewater during New York City's second wave of COVID-19: Sewershed-level trends and relationships to publicly available clinical testing data
(<https://www.medrxiv.org/content/10.1101/2022.02.08.22270666v1>)

C Hoar et al, MEDRXIV, February 9, 2022

New York City's ongoing wastewater monitoring program tracked trends in sewershed-level SARS-CoV-2 loads starting in the fall of 2020, just before the start of the City's second wave of the COVID-19 outbreak. During a five-month study period, from November 8, 2020 to April 11, 2021, viral loads in influent wastewater from each of New York City's 14 wastewater treatment plants were measured and compared to new laboratory-confirmed COVID-19 cases for the populations in each corresponding sewershed, estimated from publicly available clinical testing data. We found significant positive correlations between viral loads in wastewater and new COVID-19 cases.

- Waning 2-Dose and 3-Dose Effectiveness of mRNA Vaccines Against COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and

Vaccine effectiveness (VE) against COVID-19-associated emergency department/urgent care (ED/UC) visits and hospitalizations was higher after the third dose than after the second dose but waned with time since vaccination. During the Omicron-predominant period, VE against COVID-19-associated ED/UC visits and hospitalizations was 87% and 91%, respectively, during the 2 months after a third dose and decreased to 66% and 78% by the fourth month after a third dose. Protection against hospitalizations exceeded that against ED/UC visits.

- Safety Monitoring of COVID-19 Vaccine Booster Doses Among Adults – United States, September 22, 2021–February 6, 2022 (https://www.cdc.gov/mmwr/volumes/71/wr/mm7107e1.htm?s_cid=mm7107e1_x)

AN Hause et al, MMWR, February 11, 2022

In preauthorization trials, adverse reactions were reported less frequently following a homologous COVID-19 mRNA vaccine booster dose than after receipt of the second primary dose. Review of surveillance data found that local and systemic reactions were less frequent after a homologous COVID-19 mRNA vaccine booster dose than after the second primary vaccine dose. Myocarditis was rarely reported following an mRNA vaccine booster dose.

- Omicron BA.2 lineage spreads in clusters and is concentrated in Denmark.
(<https://pubmed.ncbi.nlm.nih.gov/35150013>)

Desingu Perumal Arumugam et al. Journal of medical virology 2022 2

The BA.2 lineage phylogenetically consists of five groups: Sweden/Denmark, Philippines, Hong Kong, India, and China. The ORF3a protein of BA.2, which is spreading in Denmark, contains a specific mutation called H78Y, and this mutation is not widely found in other countries. The Philippines, Hong Kong, India, and China groups of BA.2 also have their own unique mutations.

- Household transmission of SARS-CoV-2 Alpha variant - United States, 2021.
(<https://pubmed.ncbi.nlm.nih.gov/35147176>)

Donnelly Marisa A P et al. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2022 2

We investigated 127 households with 322 household contacts; 72 households (56.7%) had member(s) with secondary infections. SIRs were not significantly higher for Alpha (61.0% [95% confidence interval (CI) 52.4-69.0%]) than non-Alpha (55.6% [CI 44.7-65.9%], $P = 0.49$). In households with Alpha, persons who identified as Asian or Hispanic/Latino had significantly higher SIRs than those who identified as White ($P = 0.01$ and 0.03, respectively). Close contact (e.g., kissing, hugging) with primary cases was associated with increased transmission for all lineages. Persons with Alpha infection were more likely to report constitutional symptoms than persons with non-Alpha (86.9% vs. 76.8%, $P = 0.05$).

- Persistence of SARS-CoV-2 immunity, Omicron's footprints, and projections of epidemic resurgences in South African population cohorts. (<https://www.medrxiv.org/content/10.1101/2022.02.11.22270854v1>)
K Sun et al, MEDRXIV, February 13, 2022

Building on the cohort's history of past exposures to different SARS-CoV-2 variants and vaccination, we use mathematical models to explore the fitness advantage of the Omicron variant and its epidemic trajectory. Modelling suggests the Omicron wave infected a large fraction of the population, leaving a complex landscape of population immunity primed and boosted with antigenically distinct variants.

- Evaluating the effectiveness of rapid SARS-CoV-2 genome sequencing in supporting infection control teams: the COG-UK hospital-onset COVID-19 infection study (<https://www.medrxiv.org/content/10.1101/2022.02.10.22270799v1>)
O Stirrup et al, MEDRXIV, February 13, 2022

The impact of the sequencing intervention on IPC knowledge and actions, and on incidence of probable/definite hospital-acquired infections (HAIs) was evaluated. Results A total of 2170 HOCl cases were recorded from October 2020-April 2021, with sequence reports returned for 650/1320 (49.2%) during intervention phases. While we did not demonstrate a direct impact of sequencing on the incidence of nosocomial transmission, our results suggest that sequencing can inform IPC response to HOCl, particularly when returned within 5 days.

- Executable network of SARS-CoV-2-host interaction predicts drug combination treatments (<https://www.nature.com/articles/s41746-022-00561-5>)
R Howell et al, NPJ Digital Medicine, February 14, 2022

We present the first disease-stage executable signalling network model of SARS-CoV-2-host interactions used to predict effective repurposed drug combinations for treating early- and late stage severe disease. Using our executable model, we performed in silico screening of 9870 pairs of 140 potential targets and have identified nine new drug combinations. Camostat and Apilimod were predicted to be the most promising combination in effectively suppressing viral replication in the early stages of severe disease and were validated experimentally in human Caco-2 cells. Our study further demonstrates the power of executable mechanistic modelling to enable rapid pre-clinical evaluation of combination therapies tailored to disease progression.

- Effectiveness of a third dose of BNT162b2 mRNA COVID-19 vaccine in a large US health system: A retrospective cohort study ([https://www.thelancet.com/journals/lanam/article/PIIS2667-193X\(22\)00015-1/fulltext](https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(22)00015-1/fulltext))
SY Tartoff et al, The Lancet Regional Health, February 14, 2022

After only two doses, VE against infection declined from 85% (95% CI 83–86) during the first month to 49% (46–51) = 7 months following vaccination. Overall VE against hospitalization was 90% (95% CI 86–92) within one month and did not wane, however, effectiveness against hospitalization appeared to wane among immunocompromised individuals but was not statistically significant (93% [72–98] at 1

month to 74% [45–88] after = 7 months; $p=0.490$). Three-dose VE (median follow-up 1·3 months [SD 0·6]) was 88% (95% CI 86–89) against infection and 97% (95–98) against hospitalization.

- Co-infection with SARS-CoV-2 Omicron and Delta Variants Revealed by Genomic Surveillance (<https://www.medrxiv.org/content/10.1101/2022.02.13.22270755v1>)
RJ Rocket et al, MEDRXIV, February 15, 2022

We identified the co-infection of the SARS-CoV-2 Omicron and Delta variants in two epidemiologically unrelated patients with chronic kidney disease requiring haemodialysis. Both SARS-CoV-2 variants were co-circulating locally at the time of detection. Amplicon- and probe-based sequencing using short- and long-read technologies identified and quantified Omicron and Delta subpopulations in respiratory samples from the two patients.

- COVID reinfections surge during Omicron onslaught- Immunity acquired through previous infection is less effective against Omicron than against other variants, but the risk of severe COVID-19 remains low. (<https://www.nature.com/articles/d41586-022-00438-3>)
S Mallapaty, Nature, February 16, 2022

Since the Omicron variant of SARS-CoV-2 was first detected, the number of people reinfected with the coronavirus has been rising sharply – a trend that was not observed with previous variants. Researchers say that the new variant is probably driving the surge because it is able to evade the body's immune defenses.

- mRNA vaccine-induced antibodies more effective than natural immunity in neutralizing SARS-CoV-2 and its high affinity variants (<https://www.nature.com/articles/s41598-022-06629-2>)
Y Yu et al, Scientific Reports, February 16, 2022

Our data showed that N501Y RBD had fivefold higher ACE2 binding than the original variant. While some antisera from naturally infected subjects had substantially reduced neutralization ability against N501Y RBD, all blood samples from vaccinated individuals were highly effective in neutralizing it. Thus, our data indicates that mRNA vaccination may generate more neutralizing RBD antibodies than natural immunity. It further suggests a potential need to maintain high RBD antibody levels to control the more infectious SARS-CoV-2 variants.

- Response to additional COVID-19 vaccine doses in people who are immunocompromised: a rapid review ([https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(21\)00593-3/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00593-3/fulltext))
EPK Parker, The Lancet Global Health, March 2022

The extent to which additional doses enhance protection against COVID-19 among people who are immunocompromised remains uncertain. With this in mind, we did a rapid review of the safety, immunogenicity, and efficacy or effectiveness of additional vaccine doses in people who are immunocompromised, covering articles and preprints published between July 1, 2020 and Sept 27, 2021. Our aim was to capture emerging trends within the heterogeneous body of available evidence.

- Generation time of the alpha and delta SARS-CoV-2 variants: an epidemiological analysis

([https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(22\)00001-9/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00001-9/fulltext))

WS Hart et al, Lancet Inf Dis, February 2022

Between February and August, 2021, 227 households consisting of 559 participants were recruited to the UKHSA study. The alpha variant was detected or assumed to be responsible for infections in 131 households (243 infections in 334 participants) recruited in February–May, and the delta variant in 96 households (174 infections in 225 participants) in May–August. The mean intrinsic generation time was shorter for the delta variant (4.7 days, 95% credible interval [CI] 4.1–5.6) than the alpha variant (5.5 days, 4.7–6.5), with 92% posterior probability. The mean household generation time was 28% (95% CI 0–48%) shorter for the delta variant (3.2 days, 95% CI 2.5–4.2) than the alpha variant (4.5 days, 3.7–5.4), with 97.5% posterior probability.

- Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection

(https://www.nejm.org/doi/full/10.1056/NEJMoa2118691?query=featured_home)

V Hall et al, NEJM, February 16, 2022

Among previously uninfected participants who received long-interval BNT162b2 vaccine, adjusted vaccine effectiveness decreased from 85% (95% confidence interval [CI], 72 to 92) 14 to 73 days after the second dose to 51% (95% CI, 22 to 69) at a median of 201 days (interquartile range, 197 to 205) after the second dose; this effectiveness did not differ significantly between the long-interval and short-interval BNT162b2 vaccine recipients. At 14 to 73 days after the second dose, adjusted vaccine effectiveness among ChAdOx1 nCoV-19 vaccine recipients was 58% (95% CI, 23 to 77) – considerably lower than that among BNT162b2 vaccine recipients. Infection-acquired immunity waned after 1 year in unvaccinated participants but remained consistently higher than 90% in those who were subsequently vaccinated, even in persons infected more than 18 months previously.

- Effectiveness of the BNT162b2 Vaccine after Recovery from Covid-19

(https://www.nejm.org/doi/full/10.1056/NEJMoa2119497?query=featured_home)

A Hammerman et al, NEJM, February 16, 2022

A total of 149,032 patients who had recovered from SARS-CoV-2 infection met the eligibility criteria. Of these patients, 83,356 (56%) received subsequent vaccination during the 270-day study period. Reinfection occurred in 354 of the vaccinated patients (2.46 cases per 100,000 persons per day) and in 2168 of 65,676 unvaccinated patients (10.21 cases per 100,000 persons per day). Vaccine effectiveness was estimated at 82% (95% confidence interval [CI], 80 to 84) among patients who were 16 to 64 years of age and 60% (95% CI, 36 to 76) among those 65 years of age or older. No significant difference in vaccine effectiveness was found for one dose as compared with two doses.

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