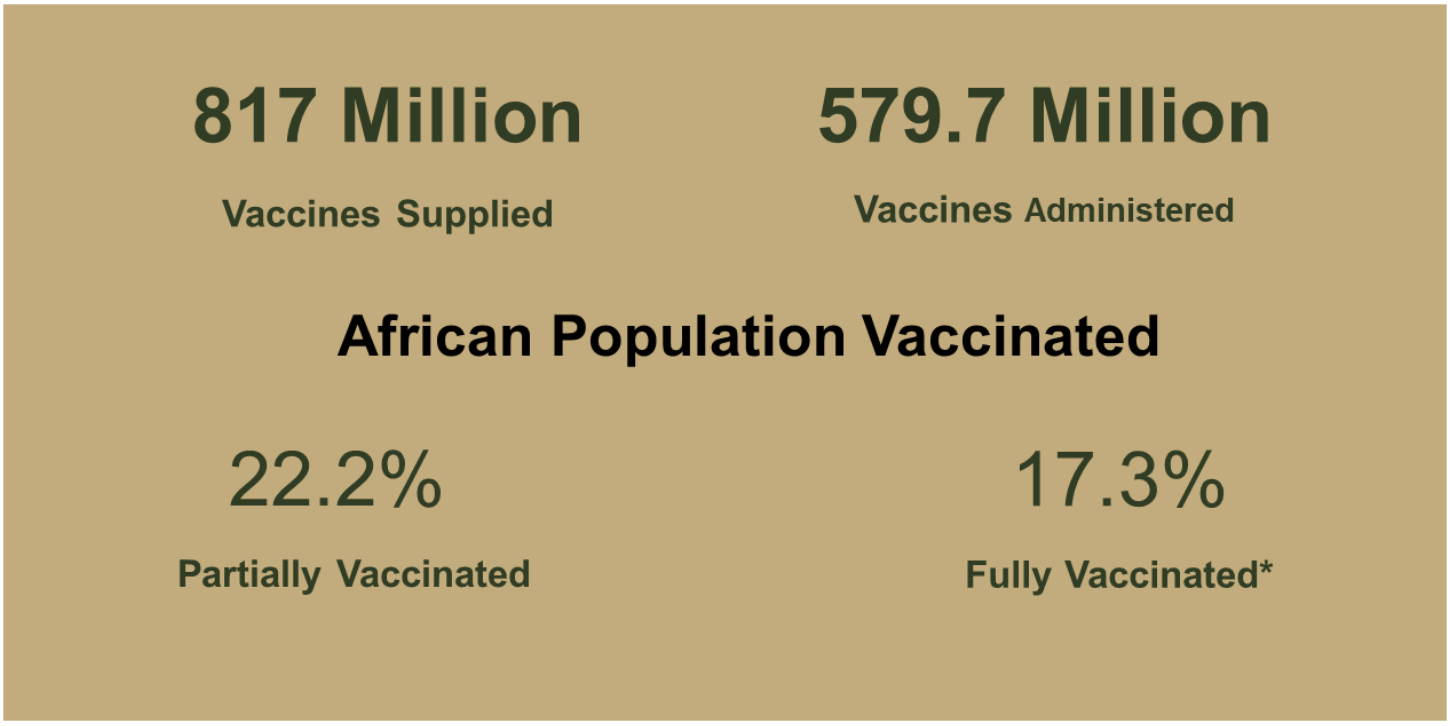
COVID-19 Scientific and Public Health Policy Update[1] (8 June 2022)

This biweekly brief details the latest developments in scientific knowledge and public health policy from around the world as well as updates to the COVID-19-related guidance from Africa CDC, WHO and other public health agencies. This brief complements the Weekly Outbreak Brief and other documents on COVID-19 and the actions that the African Union/Africa CDC and WHO/AFRO are taking to help African Union Member States. Contents are ***not intended to serve as recommendations*** *from the African Union-Africa CDC or WHO/AFRO; rather, the brief serves as a summary of the scientific information available in the public space to Member States. The outbreak is evolving rapidly and the nature of this information will continue to change. We will provide regular updates to ensure Member States are informed of the most critical developments on the science and public health best practices related to COVID-19.*

A. Trending Topics

Status of Vaccines in Africa



*Received two doses of a two-dose COVID-19 vaccine series or one dose of the Johnson & Johnson vaccine
https://africacdc.org/COVID-19-vaccination/
Updated 8 June 2022

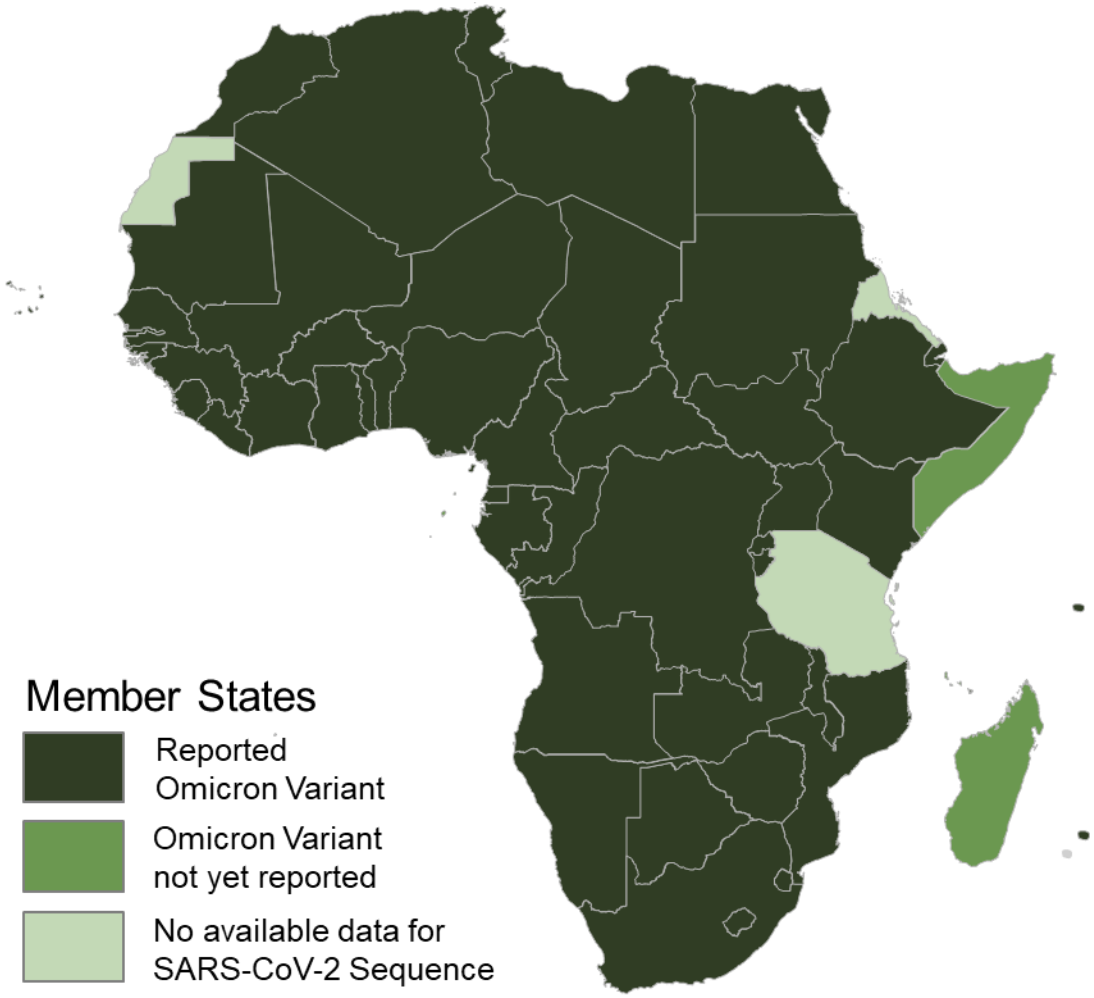
Note: Africa CDC has changed the denominator of the calculation for percentage fully vaccinated from 2020 population to 2022 population estimates (UNFPA) to give accurate projections from effective population size (Ne) perspectives.

The resulting effect is that there will be a slight reduction in fully vaccinated coverage percentages of member states and the continent at large.

[1] This update compiled for use by African Union Member States and is developed collaboratively by the African Union-Africa CDC and World Health Organization - Regional Office for Africa. **This is a preliminary summary of information and does not represent policy decisions, recommendations, or final conclusions of the African Union- Africa CDC or WHO/AFRO**.

Variants of Concern (VOC)

The Omicron variant (B.1.1.529), first reported in South Africa on 24th November 2021, has spread to 198 countries/territories/areas worldwide. As of 8 June 2022, 49 (89.1%) of the 55 Member States in Africa have reported this variant. For more information visit https://africacdc.org/institutes/africa-pathogen-genomics-initiative/.



Updated 8 June 2022

B. New guidelines and resources

Since 24 May 2022,

- Africa CDC[2] has published new guidance and resources on:
  - Africa CDC – Mastercard Foundation: Saving Lives and Livelihoods Newsletter, May 2022
  - Outbreak Brief 124: Coronavirus Disease 2019 (COVID-19) Pandemic

- U.S. CDC[3] has published new guidance and resources on:
  - Ventilation Improvement Strategies Among K–12 Public Schools — The National School COVID-19 Prevention Study
  - COVID-19 Travel Recommendations by Country

[2] Africa CDC: Africa Centres for Disease Control and Prevention
[3] U.S. CDC: United States Centers for Disease Control and Prevention

- COVID-19 Vaccines for People Vaccinated Outside the United States
- Selected Adverse Events Reported after COVID-19 Vaccination
- Operational Guidance for K-12 Schools and Early Care and Education Programs to Support Safe In-Person Learning

- WHO[4] has published new guidance and resources on:
  - Maintaining infection prevention and control measures for COVID-19 in health care facilities: Policy brief
  - Severity of disease associated with Omicron variant as compared with Delta variant in hospitalised patients with suspected or confirmed SARS-CoV-2 infection
  - Interim recommendations for the use of the Janssen Ad26.COV2.S (COVID-19) vaccine
  - Annexes to the interim recommendations for use of the Janssen Ad26.COV2.S vaccine
  - COVID-19 and mandatory vaccination: Ethical considerations

- U.S. FDA[5] has issued press releases on:
  - On 3 June, the FDA provided additional guidance to help prescribers evaluate potential drug interactions when using Paxlovid therapy for COVID-19
  - On 17 May, the FDA revised the scope of authorization for Evusheld's EUA to include new information on hypersensitivity reactions
  - As of 7 June, 438 tests and sample collection devices are authorised by the FDA under emergency use authorisations (EUAs)

- ECDC[6] has issued new resources on:
  - Technical guidance for antigenic SARS-CoV-2 monitoring
  - Communicable disease threats report, 29-4 June 2022, week 22

- UKHSA[7] has issued new guidance and press releases on:
  - COVID-19 surveillance and immunity studies
  - National technical validation process for manufacturers of SARS-CoV-2 (COVID-19) tests
  - Protocol for evaluation of rapid diagnostic assays for specific SARS-CoV-2 antigens (lateral flow devices)
  - Technical validation protocol for SARS-CoV-2 nucleic acid detection

C. Scientific updates

Basic Science

- This longitudinal study in the United States explored the mechanism underlying long COVID biology. The authors compared short and long-term systematic responses in golden hamsters following either SARS-CoV-2 or Influenza A virus (IAV) infection. They found that SARS-CoV-2 exceeded IAV in its capacity to cause permanent injury to the lung and kidney and uniquely impacted the olfactory bulb (OB) and epithelium (OE). Despite a lack of detectable infectious virus, the OB and OE demonstrated myeloid and T cell activation, proinflammatory cytokine production, and an interferon response that correlated with behavioural changes extending a month post-viral clearance. These sustained transcriptional changes could also be corroborated from tissue isolated from individuals who recovered from COVID-19. Their findings highlight a molecular mechanism for persistent COVID-19 symptomology and provide a model to explore future therapeutics.

[4] WHO: World Health Organization
[5] U.S. FDA: United States Food and Drug Administration
[6] ECDC: European Centre for Disease Prevention and Control
[7] UKHSA: United Kingdom Health Security Agency

- This in-vivo animal model study in Taiwan monitored remdesivir and its metabolites in maternal blood, fetus, placenta and amniotic fluid of pregnant rats. The authors developed a multiple microdialysis sampling system coupled with ultra-high performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS) to assay and monitor remdesivir and GS-441524 deposition. Remdesivir is rapidly bio-transformed into GS-441524 in the maternal blood, which then readily crossed the placenta with a mother-to-fetus transfer ratio of 0.51 ± 0.18. The C_{max} and AUC_{last} values of GS-441524 followed the order: maternal blood > amniotic fluid > fetus > placenta in rats. These findings suggest that careful consideration should be taken for the use of remdesivir in the treatment of COVID-19 in pregnancy.

Vaccines

- This nationwide register-based cohort study in Norway assessed whether COVID-19 vaccination in pregnancy was associated with reduced risk of COVID-19 in infants up to age 4 months during periods dominated by Delta and Omicron variants. The study involved 21,643 live-born infants of which 9,739 (45%) were born to women who received a second or third dose of a COVID-19 vaccine during pregnancy. The first 4 months of life incidence rate of a positive test for SARS-CoV-2 was 5.8 per 10,000 follow-up days. Infants of mothers vaccinated during pregnancy had a lower risk of a positive test compared with infants of unvaccinated mothers and lower risk during the Delta variant–dominated period (incidence rate, 1.2 vs 3.0 per 10,000 follow-up days; adjusted hazard ratio, 0.29; 95% CI, 0.19-0.46) compared with the Omicron period (incidence rate, 7.0 vs 10.9 per 10,000 follow-up days; adjusted hazard ratio, 0.67; 95% CI, 0.57-0.79). Maternal COVID-19 vaccination may provide passive protection to young infants, for whom COVID-19 vaccines are currently not available.
- This cross-sectional study in Japan examined the associations between sex and age and susceptibility of delayed large local reactions (DLLRs) after injection of the SARS-CoV-2 mRNA-1273 vaccine. The study involved 5,893 participants. A total of 747 participants (12.7%) experienced DLLR symptoms after the first dose of the mRNA-1273 vaccine. Symptoms were mild and not considered as contraindications to the vaccine. The incidence rate was significantly higher among females (22.4% [577 participants]; OR, 5.30; 95% CI, 4.42-6.34) than among males (5.1% [170 participants]). Moreover, the incidence rate was significantly higher among participants aged 30 to 39 years (14.3% [129 participants]; OR, 1.68; 95% CI, 1.25-2.26) than among participants aged 18 to 29 years (9.0% [81 participants]). These findings suggest that DLLR may be a type IV allergic skin reaction.
- This prospective cohort study in Switzerland describes early adverse events and perinatal outcomes in pregnant women who received at least one dose of mRNA vaccine. The study involved 1012 vaccinated women, 894 (88·3%) received both injections during pregnancy, with BNT162b2 (*n* = 271) or mRNA-1273 (*n* = 623) vaccines. Local events were reported in 81.3% and 80.5% after the first and second doses. Rates of systemic reactions (mainly fatigue and headache) were similar after the first dose and most frequent after the second dose of mRNA-1273. Four (0.4%; 95%CI [0.1-1.0]) severe early adverse events occurred: pulmonary embolism, preterm premature rupture of membranes, isolated fever with hospitalisation, and herpes zoster. Of 107 patients vaccinated before 14 weeks, one (0.9%; 95%CI [0.0-5.1]) early spontaneous abortions was reported (at 8 weeks). Of 228 vaccinated before 20 weeks one (0.4%; 95%CI [0.0-2.4]) late spontaneous abortion was reported (at 16 weeks). Of 513 women exposed before 37 weeks, 33 (6.4%; 95%CI [4.5-8.9]) delivered preterm. Among 530 patients exposed in pregnancy, no stillbirth was reported.

Diagnostics

- This study in Hong Kong describes a decentralized, instrument-free microfluidic device that directly visualizes SARS-CoV-2 antibody levels. Magnetic microparticles (MMPs) and polystyrene microparticles (PMPs) can bind to SARS-CoV-2 antibodies simultaneously. In a microfluidic chip, this binding reduces the incidence of free PMPs escaping from magnetic separation and shortens PMP accumulation length at a particle dam. This visual quantitative result enables use in either sensitive mode [limit of detection (LOD): 13.3 ng/ml; sample-to-answer time: 70 min] or rapid mode (LOD: 57.8 ng/ml; sample-to-answer time: 20 min) and closely agrees with the gold standard enzyme-linked

immunosorbent assay. Trials on 91 vaccinees revealed higher antibody levels in mRNA vaccinees than in inactivated vaccinees and their decay in 45 days, demonstrating the need for point-of-care devices to monitor immune protection.

- This study in the United States describes the development of a quantitative and ultrasensitive in situ immunoassay technology for SARS-CoV-2 detection in saliva (QUIT SARS-CoV-2). Their nanoporous membrane resonator generates a rapid oscillating flow to purify and concentrate fully intact SARS-CoV-2 virus in saliva by 40-fold for in situ detection of viral antigens based on chemiluminescent immunoassay within 20 minutes. This method can not only achieve a detection sensitivity below 100 copies/ml of the virus, comparable to the bench-top PCR equipment; it can also improve detection specificity via direct monitoring of viral loads. The integrated portable QUIT SARS-CoV-2 system, which enables rapid and accurate on-site viral screening with a high-throughput sample pooling strategy, can be performed in primary care settings and substantially improve the detection and prevention of COVID-19.
- This study in Australia assessed the clinical sensitivity and specificity of the Abbott PanBio™ COVID-19 Ag test (RAT) and described the clinical pathway of patients who received rapid antigen testing in the emergency department (ED). The study involved 1762 paired RAT/RT-PCR samples. The overall sensitivity of 75.5% (206/273; 95% CI: 69·9-80·4) was found for RAT, with specificity of 100% (1489/1489; 95% CI: 99·8-100). Sensitivity improved with increasing risk for COVID-19 infection, from 72·4% (95% CI: 52·8-87·3) in the 'No Risk' cohort to 100% (95% CI: 29·2-100) in the 'High Risk' group. Time in the ED for the 'At/High Risk' group decreased from 421 minutes (IQR: 281, 525) for those with a positive RAT result to 274 minutes (IQR:140, 425) for those with a negative RAT result, p = 0.02. Their findings support a role for RAT to streamline COVID-19 positive patient flow in a hospital setting.

Care and Treatment

- This case series in Nigeria presents the varied manifestations of multisystemic inflammatory syndrome in children (MIS-C). The study involved 28 children and adolescents across 9 facilities in Lagos between July 2020 and July 2021. Mucocutaneous, gastrointestinal and cardiovascular manifestations were identified in 75.0%, 71.4% and 89.3% of patients respectively. Acute kidney injury and aseptic meningitis were noted in 32.1% and 17.9% of patients respectively. Cardiac manifestations at presentation included coronary dilatation and pericardial effusion in 46.4% each, ventricular dysfunction (32.1%), atrioventricular valve regurgitation (25.0%), prolonged QTc interval (40.0%) and first-degree atrioventricular block (16.0%). Therapy included aspirin in 89.3%, steroids in 75.0% and intravenous immunoglobulin infusion in 60.7%. All patients survived and were discharged after a mean of 11.14 (SD 5.65) days. Frequency of coronary dilatation had reduced from 46.4% to 7.1% by 3 months follow up and prolonged QTc interval persisted until the 6-week follow up in 4.5% of patients. Echocardiogram and electrocardiogram findings were normal in all patients assessed at 6 months follow up.
- This systematic review and meta-analysis summarised the potential risk factors for impaired diffusing capacity for carbon monoxide (DLCO) in convalescent COVID-19 patients. The systematic review and meta-analysis included 18 and 12 studies respectively. The percentage of abnormal DLCO among recovered COVID-19 subjects who underwent follow-up ranged from 14% to 67%. Risk factors for impaired DLCO included female (OR: 4.011; 95% CI: 2.928–5.495), altered chest computerized tomography (CT) (OR: 3.002; 95% CI: 1.319–6.835), age (OR: 1.018; 95% CI: 1.007–1.030), higher D-dimer levels (OR: 1.012; 95% CI: 1.001–1.023) and urea nitrogen (OR: 1.004;95% CI: 1.002–1.007). Raising awareness and implementing interventions for possible modifiable risk factors may be valuable for pulmonary rehabilitation.
- This meta-analysis of four randomised clinical trials assessed the role of baricitinib in hospitalised patients with COVID-19. The 4 studies involved a total of 10,815 patients. Pooled analysis using random-effects model showed a statistically significant reduction in 28-day mortality (OR 0.69, 95% CI 0.50-0.94; p=0.04, I^2=65%) and composite outcome of progression to severe disease needing positive pressure ventilation, invasive mechanical ventilation (IMV) or death (OR 0.89, 95% CI 0.80-0.99, p= 0.03, I^2=0%). There was a favourable trend towards reduced progression to IMV or ECMO (OR 0.76,

95% CI 0.58-1.01; p=0.06, I^2=49%) in the baricitinib arm compared to standard therapy, even though it was not statistically significant. Statistical significance was achieved for all outcomes with fixed-effects model analysis.

- This single-centre, prospective, open-label phase 3 trial assessed the effectiveness of favipravir, camostat, and ciclesonide combination therapy in patients with moderate COVID-19 pneumonia. The study enrolled 121 patients, 56 received monotherapy (favirapir) and 61 received combination therapy. The median time of hospitalisation was 10 days for the combination and 11 days for the monotherapy group. The median time to discharge was statistically significantly lower in the combination therapy vs monotherapy group (HR, 1.67 (95% CI 1.03–2.7; P = 0.035). The hospital discharge rate was statistically significantly higher in the combination therapy vs monotherapy group in patients with less severe COVID-19 infections and those who were ≤60 years. There were no significant differences in clinical findings between the groups at 4, 8, 11, 15, and 29 days. Adverse events were comparable between the groups. There were two deaths, with one in each group.
- This randomised, placebo-controlled, double-blind, head-to-head trial assessed the combination of baricitinib plus remdesivir versus dexamethasone plus remdesivir in preventing progression to mechanical ventilation or death in hospitalised patients with COVID-19. The study involved 1010 patients who were enrolled from 67 sites across the USA, South Korea, Mexico, Singapore and Japan. Mechanical ventilation-free survival by day 29 was similar between the study groups (Kaplan-Meier estimates of 87.0% [95% CI 83.7 to 89.6] in the baricitinib plus remdesivir plus placebo group and 87.6% [84.2 to 90.3] in the dexamethasone plus remdesivir plus placebo group; risk difference 0.6 [95% CI −3.6 to 4.8]; p=0.91). Dexamethasone was associated with significantly more adverse events, treatment-related adverse events, and severe or life-threatening adverse events.

Epidemiology

- This modelling study across 47 countries of the WHO African region assessed COVID-19 transmission dynamics since the beginning of the pandemic and throughout 2022. Their model estimates the number of SARS-CoV-2 infections in the African region to be 505.6 million (95% CI 476.0–536.2), inferring that only 1.4% (1/71) of SARS-CoV-2 infections in the region were reported. Deaths were estimated at 439,500 (95% CI 344,374–574,785), with 35.3% (1/3) of these reported as COVID-19-related deaths. Although the number of infections were similar between 2020 and 2021, 81% of the deaths were in 2021. 52.3% (95% CI 43·5–95·2) of the region's population is estimated to have had some SARS-CoV-2 immunity, given vaccination coverage of 14.7% as of 31 December 2021. By the end of 2022, they estimate that infections will remain high, at around 166.2 million (95% CI 157·5–174·9) infections, but deaths will substantially reduce to 22,563 (14,970–38,831). There is a need for surveillance of hospitalisations, comorbidities, and the emergence of new variants of concern, and scale-up of representative seroprevalence studies, as core response strategies.
- This study in Uganda performed SARS-CoV-2 whole-genome sequencing for 266 naso/oropharyngeal samples collected during June–December 2021 from 28 travellers arriving at Entebbe International Airport and from 238 patients in Uganda from 18 districts. Genomic sequencing revealed that the Delta variant was the dominant virus. However, the Omicron variant emerged in late November 2021 from travellers arriving through Entebbe International Airport (39.29% from South Africa, 28.57% from Nigeria, 14.29% from Kenya, 7.14% from the Democratic Republic of the Congo, 3.57% from Ethiopia, 3.57% Rwanda, and 3.57% from the United States), and Omicron community transmissions are increasing (based on PCR genotyping). Their results highlight the need for surveillance and infection control measures to prevent future pandemic waves.
- This prospective cohort study in South Africa assessed the kinetics of viral shedding, transmission dynamics, and persistence of immunity conferred by sequential exposures to different SARS-CoV-2 variants. The study involved 638 and 557 participants in a rural and urban site respectively. The authors found durable cross-protective immunity conferred by prior infection against pre-Omicron variants. However, Omicron successfully breached population immunity due to a combination immune escape and increased transmissibility, reinfecting a large fraction (44% - 81%) of the population and leaving a

complex immune landscape of population immunity primed and boosted with antigenically distinct variants.

- This cross-sectional study in South Africa assessed the COVID-19 seroprevalence among blood donors. The authors analysed 3,395 samples obtained in mid-March 2022 from all provinces of South Africa. They found no evidence of age and sex dependence on prevalence, but there was significant variation by race. The race-weighted national extrapolation is that 98% of South Africans have some antibodies, noting that 10% have anti-spike antibodies but not anti-nucleocapsid antibodies. [*not peer reviewed*]
- This cohort study in South Korea compared the secondary attack rate and infectious viral shedding kinetics of SARS-CoV-2 between fully vaccinated individuals (breakthrough infection group) and partially or unvaccinated individuals (non-breakthrough infection group). The study involved 173 individuals with COVID-19, of whom 50 (29%) had a breakthrough infection. Secondary transmission was significantly less common in the breakthrough infection group than in the non-breakthrough infection group (3/43 [7%] vs 29/110 [26%]; p = .008). In the viral shedding kinetics study, 45 patients infected with the Delta variant were included, of whom 6 (13%) were fully vaccinated and 39 (87%) were partially or unvaccinated. Viable virus in cell culture was detected for a notably longer duration in partially vaccinated (8 days after symptom onset) or unvaccinated (10 days after symptom onset) individuals compared with fully vaccinated individuals (4 days after symptom onset). Results from this study provide important evidence that despite the possibility of breakthrough infections, COVID-19 vaccinations remain critically useful for controlling the spread of SARS-CoV-2.
- This modelling study in the United States describes the development of PyR_0, a hierarchical Bayesian multinomial logistic regression model that infers the relative prevalence of all viral lineages across geographic regions, detects lineages increasing in prevalence, and identifies mutations relevant to fitness. The authors applied PyR_0 to all publicly available SARS-CoV-2 genomes (6,466,300) and identified numerous substitutions that increase fitness, including previously identified spike mutations and many non-spike mutations within the nucleocapsid and non-structural proteins. PyR_0 forecasts the growth of new lineages from their mutational profile, ranks the fitness of lineages as new sequences become available, and prioritises mutations of biological and public health concerns for functional characterization.

Infection Prevention & Control

- This study in Australia assessed transmission dynamics among healthcare workers (HCW). The authors performed state-wide SARS-CoV-2 genomic epidemiological investigations. The study involved 765 HCW with COVID-19. Genomic sequencing was successful for 612 (80%) cases. Thirty-six investigations were undertaken across 12 healthcare facilities (HCFs). Genomic analysis revealed that multiple introductions of COVID-19 into facilities (31/36) were more common than single introductions (5/36). Major contributors to HCW acquisitions included mobility of staff and patients between wards and facilities and characteristics and behaviours of patients that generated numerous secondary infections. Key limitations at the HCF level were identified. Their findings provide insight into how sequencing laboratories can work together with healthcare infection control staff to provide actionable results with public health implications during an active pandemic.
- This systematic review summarises the emission profiles of the droplets from different respiratory activities, including emission rates, size distributions and initial velocities; the dynamics of droplets in indoor environment; the infection risk of COVID-19 in public transport; and the factors influencing the virus transmission. The authors recommend further investigations based on field measurements and modelling studies into the influence of different ventilation systems on the transmission rate in public transport, which would provide the scientific basis for controlling the transmission of diseases.

Non-pharmaceutical interventions, social distancing

- This study in South Korea assessed changes in respiratory viruses other than SARS-CoV-2 that occurred following the implementation of non-pharmacological interventions (NPIs) during the COVID-

19 pandemic. The study involved analysis of samples from 3,334 participants that presented with influenza-like illness from January 2018 to December 2021. After NPIs were implemented, the detection of respiratory viruses other than SARS-CoV-2 decreased overall. The yearly detection rate of respiratory viruses decreased from 69.5% (399/574) in 2018 and 73.3% (505/689) in 2019 to 19.8% (206/1,043) in 2020 and 34.9% (365/1,028) in 2021. The epidemic was more prominent in respiratory viruses such as human influenza virus and respiratory syncytial virus, which were considered dominant viruses. The authors recommend further studies on the detection of viruses and changes in the actual infection patterns before and after the implementation of NPIs.

- This modelling study in France analysed a closely monitored SARS-CoV-2 outbreak in a hospital in early 2020 and estimated the patient-to-patient transmission rate and basic reproduction number (R_0). Their model accounted for stochastic effects and undetected infections and was fit to patient test results. The model took into account changes in testing capacity over time, and for the evolving PCR sensitivity at different stages of infection. R_0 estimates varied considerably across wards, ranging from 3 to 15 in different wards. During the outbreak, the hospital introduced a contact precautions policy. The results strongly support a reduction in the hospital-level R_0 after this policy was implemented, from 8.7 to 1.3, corresponding to a policy efficacy of 85% and demonstrating the effectiveness of non-pharmaceutical interventions.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 7 June, Novavax announced the U.S. Food and Drug Administration (FDA) Vaccines and Related Biological Products Advisory Committee (VRBPAC) had positive recommendation that the FDA grant Emergency Use Authorization (EUA) for the Novavax COVID-19 vaccine (NVX-CoV2373) for individuals aged 18 years and over. The recommendation was based on data from the pivotal Phase 3 clinical trial, PREVENT-19, which enrolled approximately 30,000 participants aged 18 years and older in the U.S. and Mexico. In the trial, the Novavax COVID-19 vaccine demonstrated 90.4% efficacy (95% confidence interval [CI], 82.9 to 94.6; p<0.001) with a reassuring safety profile. Serious and severe adverse events were low in number and balanced between vaccine and placebo groups. The most common adverse reactions observed during the trial (frequency category of very common ≥1/10) were headache, nausea or vomiting, myalgia, arthralgia, injection site tenderness/pain, fatigue, and malaise. The data showed that overall, the rate of myocarditis was balanced between the vaccine and placebo arms (0.007% and 0.005%) and in the post-crossover portions of Novavax trials the observed cases were all within the expected rate. Clinical trial registration #: (NCT04611802).
- On 25 May, Codagenix announced the first patient has been dosed in a U.K.-based Phase 1 clinical trial to evaluate the use of Codagenix's novel intranasal, live-attenuated virus vaccine, CoviLiv, as a booster in healthy adults following prior vaccination with approved COVID-19 vaccines. The phase 1 trial is evaluating the safety and immunogenicity of CoviLiv as a heterologous booster in approximately 30 healthy adults who have been previously vaccinated against COVID-19 with an authorized mRNA or adenovirus-vectored vaccine. Primary outcome measures for the study include humoral immunogenicity, as determined by immunoglobulin G (IgG) and neutralising antibody concentrations at days 1, 29, and 181 post-administration. The study will also measure viral shedding on days 4 and 8 as an early gauge of booster efficacy. Previous clinical studies of CoviLiv as a primary vaccine indicate that it stimulates strong cellular immune responses and blocks nasal replication following a single intranasally administered dose, offering the potential to prevent viral transmission through induction of mucosal immunity in the nose. CoviLiv demonstrates its potential as a broadly protective vaccine as it significantly provides immune responses to SARS-CoV-2 spike and non-spike proteins. Clinical trial registration #: (NCT05233826).

Therapeutics trials:

- On 7 June, Veru announced it has submitted an emergency use authorization (EUA) application to the U.S. Food and Drug Administration for its sabizabulin oral 9mg treatment of moderate to severe hospitalised COVID-19 patients at high risk for developing Acute Respiratory Distress Syndrome

(ARDS). The submission based on the positive results from the double-blind, randomised, multicentre placebo-controlled Phase 3 COVID-19 clinical trial evaluating the efficacy and safety of sabizabulin, an oral, first-in-class, new chemical entity, cytoskeleton disruptor that has dual anti-inflammatory and antiviral properties, in approximately 204 hospitalised COVID-19 patients with moderate to severe COVID (≥ WHO 4-supplemental oxygen) at high risk for ARDS and death. The primary efficacy endpoint was the proportion of deaths by Day 60. Based on a planned interim analysis of the first 150 patients randomised, the Independent Data Monitoring Committee unanimously halted the study for overwhelming efficacy which showed that sabizabulin 9 mg once daily treatment resulted in a clinically meaningful and statistically significant 55.2% relative reduction in deaths. Sabizabulin was well tolerated. Clinical trial registration #: (NCT04842747).

- On 3 June, Sorrento Therapeutics announced the first subject was dosed in a Phase I clinical study of its oral main viral protease (Mpro) inhibitor, STI-1558. STI-1558 is a potent Mpro inhibitor with an IC50 value of 2.7 nM and has demonstrated potent antiviral activity against all COVID-19 variants studied, including Omicron, with an IC90 value between 14 nM and 41 nM (an IC50/IC90 is the concentration of drug need to produce a 50%/90% inhibition of activity) in vitro following infection of human bronchial epithelial cells. It is also a Cathepsin L inhibitor, which may block effective viral entry into host cells. In preclinical studies, STI-1558 showed an oral antiviral activity against SARS-CoV-2 in a humanized transgenic mice model. The Phase I study is conducted in Australia to evaluate the safety, tolerability, and pharmacokinetics of STI-1558 in single ascending doses (SAD) followed by multiple ascending doses (MAD) compared to placebo in healthy volunteers. Clinical trial registration #: (NCT05364840).
- On 1 June, Adamis Pharmaceuticals Corporation announced that the Data Safety Monitoring Board (DSMB) overseeing the Phase 2/3 clinical trial investigating the use of Tempol for the treatment of COVID-19, determined that the study can continue as planned based on an interim review of the data on clinical and safety of the trial. The phase 2/3 trial is adaptive, randomised, double-blind, placebo-controlled enrolling high risk subjects with early COVID19 infection with a primary endpoint of limiting hospitalisation. Approximately 248 subjects > 18 years of age diagnosed with COVID-19 infection will be enrolled and they will all receive standard of care. Eligible subjects with positively diagnosed COVID-19 infection are randomised 1:1 to receive either Tempol or placebo. Clinical trial registration #: (NCT04729595).
- On 30 May, Biotron has obtained positive guidance from the US Food and Drug Administration (FDA) on the design of the Phase 2 clinical trial of its lead antiviral drug, BIT225, to potentially treat Covid-19 in adults. This package comprised an overview of preclinical and clinical development and particular queries linked to regulatory needs for advancing to submitting an investigational new drug (IND) application for the therapy. The guidance was sought for the design of the Phase 2 trial in newly diagnosed Covid-19 patients and assuring that the preclinical data package and production processes were sufficient to back this trial.
- On 26 May, Moleculin Biotech, announced the commencement of dosing in its first-in-human Phase 1a study to evaluate the safety and pharmacokinetics (PK) of WP1122 in healthy volunteers for the treatment of COVID-19 (MB-301). WP1122 is recently received IND clearance from the U.S. Food and Drug Administration (FDA) to initiate a Phase 1 study of WP1122 for the treatment of Glioblastoma Multiforme (GBM). It is a metabolism/glycosylation inhibitor, a prodrug of a well-known glucose decoy called 2-deoxy-D-glucose (2-DG). WP1122 was developed as a 2-DG prodrug to provide a more favourable pharmacological profile and was found to have greater potency than 2-DG alone in preclinical models where tumor cells require higher glycolytic activity than normal cells. WP1122 has also been shown to have a greater antiviral effect than 2-DG against SARS-CoV-2 in MRC-5 cells in culture. The Phase 1a, first-in-human, randomised, double-blind, placebo-controlled, overlapping single ascending doses (SAD) and multiple ascending doses (MAD) will investigate the effects of WP1122 administered as an oral solution in healthy human volunteers in the United Kingdom. Dose escalation will take place in sequential SAD cohorts, and MAD will start as soon as SAD has completed at least 3 dosing cohorts in which WP1122 is found to be safe and well-tolerated. This study in healthy volunteers will explore safety and PK, and subsequent antiviral clinical development will be in patients infected with SARS-CoV-2 to further evaluate safety and establish a favourable risk/benefit profile. Dose escalation, during the SAD portion of this study, will proceed up to a maximum dose of 64 mg/kg

as a single dose. Dosing of WP1122 will start in SAD at 8 mg/kg as a single dose and escalate in two-fold increments (i.e. to 16 then 32 mg/kg as single doses, etc.) in subsequent cohorts. Dosing of WP1122 in the MAD cohorts will start after a dose of 32 mg/kg has been achieved in the single dose cohort. The first dose administered in MAD will be 16 mg/kg every 12 hours (32 mg/kg/day) for 7 days and dosing in the second MAD cohort will escalate to 32 mg/kg every 12 hours (64 mg/kg/day) for 7 days. Approximately 80 subjects are expected to be enrolled in this trial. Clinical trial registration #: (NCT05195723).

- On 25 May, NRx Pharmaceuticals announced results of a review conducted by the Data Safety and Monitoring Board. The DSMB reviewed data of approximately 460 patients with Critical COVID-19 Respiratory Failure who were enrolled in the ACTIV-3b (TESICO) trial, most of which had reached the 90-day endpoint. The DSMB recommended stopping further randomisation to aviptadil due to aviptadil not meeting the futility guidelines outlined by the pre-approved analytical plan. The primary endpoint (90 day 6-category ordinal score) was not supportive (OR 1.10; 0.79 – 1.54; p=0.56), and 90-day mortality secondary endpoint was also not supportive with 37% mortality in the aviptadil group vs 36% in the placebo group; HR 1.04 (0.77-1.41); p=0.79. There were no safety concerns, the known side effects of aviptadil (principally diarrhoea and hypotension) were managed well with the protocols in place. Clinical trial registration #: (NCT04311697).
- On 24 May, Shanghai Junshi Biosciences announced that the Phase 3 clinical study comparing the efficacy and safety of VV116 (JT001) and nirmatrelvir/ritonavir ("PAXLOVID") in the treatment of patients with mild to moderate COVID-19 who are at high risk for progression to severe COVID-19 including death, has reached its pre-specified primary endpoint and secondary efficacy endpoint. VV116 (JT001) is a new investigational oral drug nucleoside analogue that can inhibit the replication of anti-SARS-CoV-2. The phase 3 study is a multicentre, single-blind, randomised, controlled to evaluate the efficacy and safety of VV116 (JT001) in comparison with PAXLOVID in the early treatment of patients with mild to moderate COVID-19 who are at high risk for progression to severe COVID-19 and death. A total of 822 patients were enrolled and a single-blind design was adopted to conceal the distribution of therapeutic drugs to both the investigators (including the endpoint evaluator) and the study sponsor. The primary endpoint was "time to sustained clinical recovery," and the secondary endpoints included "percentage of participants who had progression of COVID-19 (defined as progression to severe and/or critical COVID-19 and death from any cause) by Day 28", "time to sustained disappearance of clinical symptoms", and "percentage of participants who turned negative for SARS-CoV-2". The study results show that compared to PAXLOVID, VV116 (JT001) provided patients with a shorter median time to sustained clinical recovery, achieving statistical superiority. It has a good safety profile, and its overall incidence of adverse events (AE) is lower than that of PAXLOVID. Clinical trial registration #: (NCT05341609).
- On 24 May, Insilico Medicine announced its nomination of a novel preclinical candidate (PCC) targeting 3C-like (3CL) protease for the treatment of COVID-19. Insilico's PCC is an orally available 3CL protease inhibitor with a novel structure generated using Insilico's AI platform. Insilico's candidate demonstrated a favourable profile with good in vivo efficacy at low doses, efficient synthesis, and no need for co-administration with Ritonavir. It also showed broad-spectrum antiviral activities, not only for SARS-CoV-2 and its variants, but also for other types of coronaviruses that cause diseases including severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).

Immunotherapies trials:

- On 2 June, Bristol Myers Squibb announced topline results from the Phase 3 Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV-1) Immune Modulators clinical trial. Orencia (abatacept) is a selective costimulation modulator that disrupts the continuous cycle of T-cell activation. It is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA), patients 2 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA) and adult patients with active psoriatic arthritis (PsA). The phase 3 study evaluated the safety and efficacy of a single dose of immune modulators, including Orencia (abatacept) IV (10 mg/kg) versus placebo when given with standard of care to determine if modulating the immune system's response could speed recovery and reduce death in adults hospitalised with moderate to

severe COVID-19. Treatment with Orencia versus placebo displayed a strong but not statistically significant improvement in the primary endpoint of time to recovery as measured by the day of hospital discharge. Analyses of the secondary endpoints, which included mortality and clinical status, demonstrated Orencia reduced participants' risk of death and improved their clinical status at 28 days after entering the study when compared with placebo. The risk of death was lower for participants who received Orencia at 11%, versus 15% for those who received placebo, and the odds of dying were 37.4% lower. The relative improvement in mortality was similar in both moderately and severely ill participants. People in the Orencia group had 34.2% better odds of clinical improvement than those in the placebo group. The safety profile of Orencia remained consistent, with no new safety signals reported in the study. Clinical trial registration #: (NCT04593940).

- On 26 May, Taiwanese biotech - AcadeMab announced new development of COVID immunotherapies through the development of a potentially life-saving monoclonal antibody for COVID-19 patients using single B cell technology. The new therapy treatment specifically targets the SARS-CoV-2 Omicron variant – currently the most common strain of COVID-19 infections around the world. Studies conducted by AcadeMab have found high efficacy of their human monoclonal antibodies against the Omicron variant within 4 months. In one of their studies, it was found that one human antibody showed the best neutralisation ability (IC50 = 11.4 and 4.3 ng/ml) in both Omicron variants BA.1 and BA.2 respectively.

Contributors

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