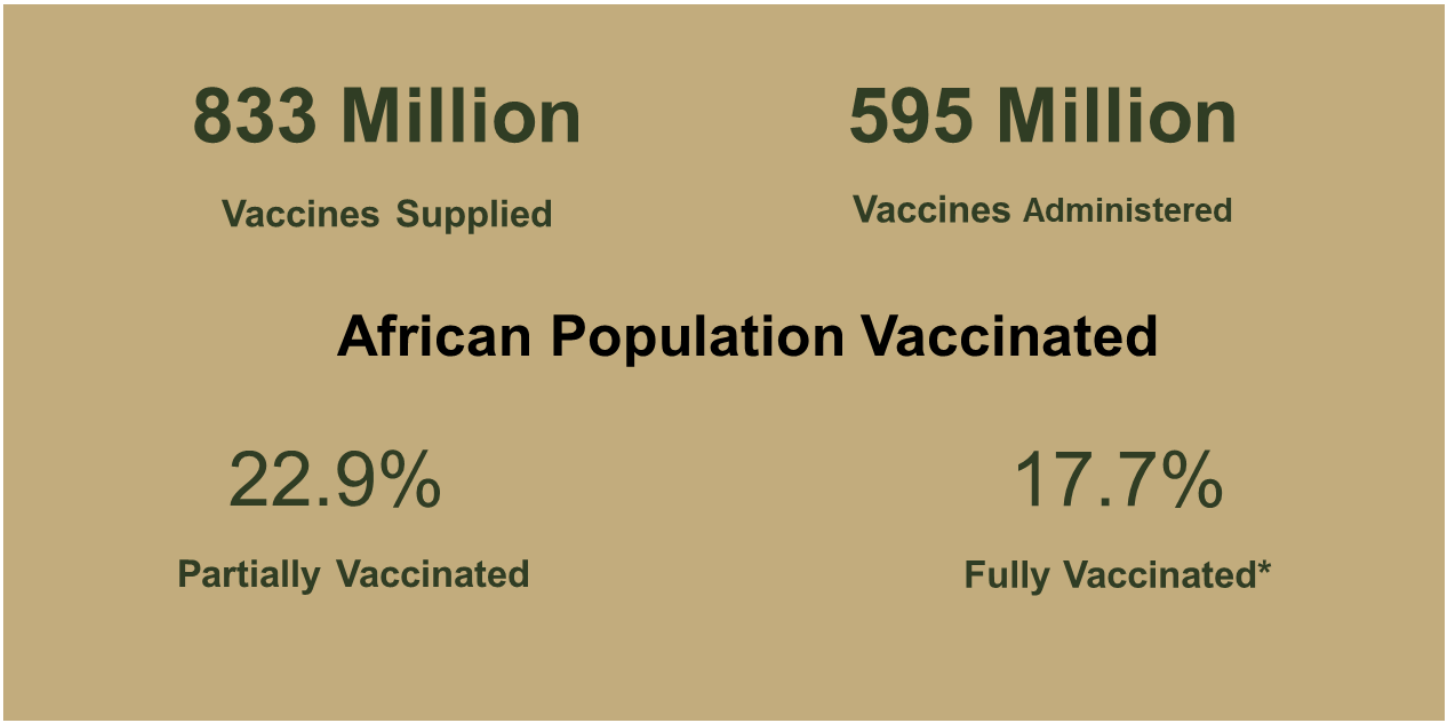
COVID-19 Scientific and Public Health Policy Update[1] (22 June 2022)

This bi-weekly 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 22 June 2022

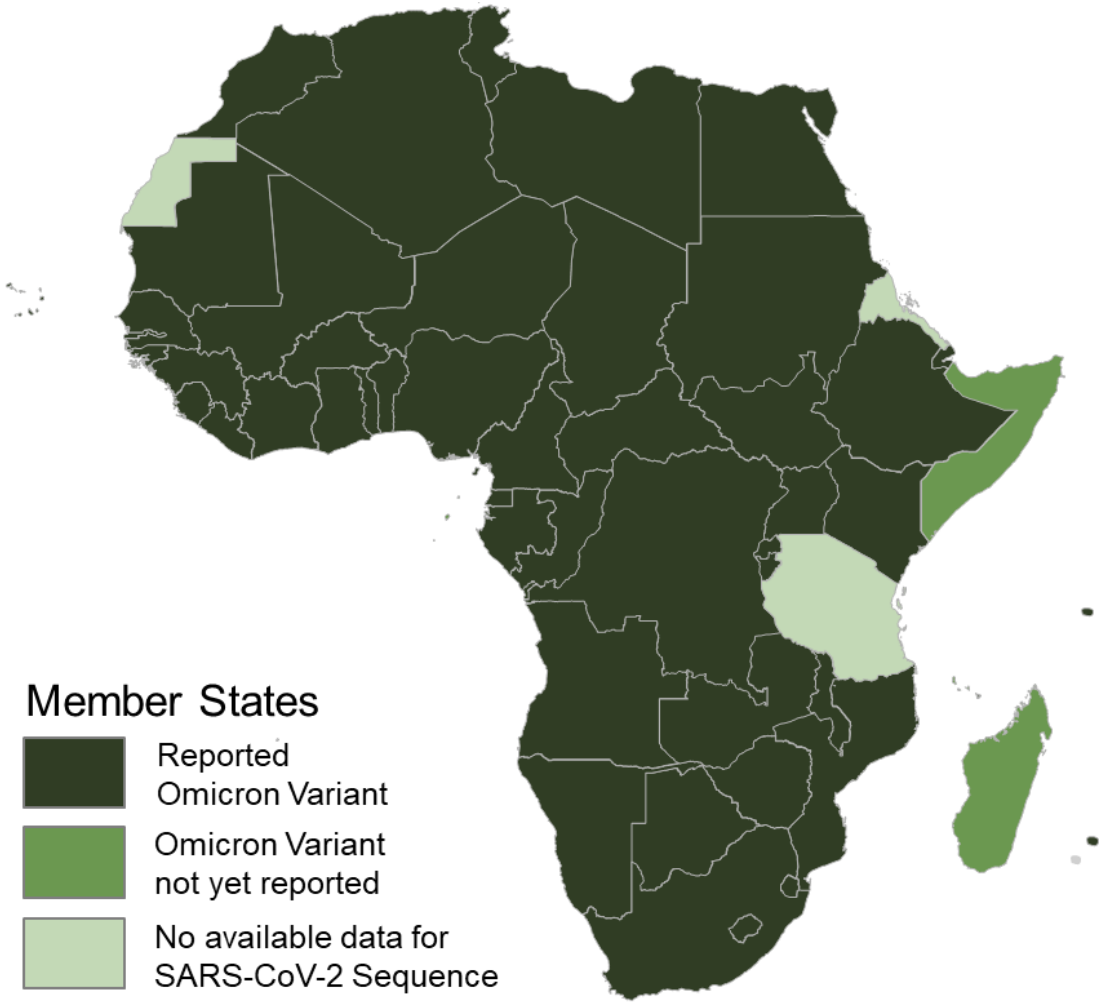
Note: Africa CDC has changed the denominator of the calculation for percentage fully vaccinated from 2020 population to 2022 population estimates (UNFPA) to give accurate projections from effective population size (Ne) perspectives.

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 22 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 22 June 2022

B. New guidelines and resources

Since 7 June 2022,

- Africa CDC[2] has published new guidance and resources on:
  - Africa CDC Support Program to Combat COVID-19 and Future Public Health Risks
  - Outbreak Brief 126: Coronavirus Disease 2019 (COVID-19) Pandemic
  - Infection Prevention and Control (IPC) Standard Operating Procedure (SOP) for Training/Meetings in the context of COVID-19

- U.S. CDC[3] has published new guidance and resources on:

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

- Operational Considerations for Maintaining Essential Services for and Providing Maternal, Newborn, and Child Healthcare in Low-Resource Countries
- Post-COVID Conditions: CDC Science
- COVID-19 Vaccine Recommendations for Children and Teens
- Frequently Asked Questions about COVID-19 Vaccination in Children
- Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination

- WHO[4] has published new guidance and resources on:
  - Meeting of the Strategic Advisory Group of Experts on Immunization, April 2022: conclusions and recommendations
  - WHO mass gathering COVID-19 risk assessment tool: generic events, version 3
  - WHO consultation to adapt influenza sentinel surveillance systems to include COVID-19 virological surveillance
  - Integrated sentinel surveillance of influenza and SARS-CoV-2 and the development of the Global Influenza Surveillance and Response System Plus
  - Role of the polio network in COVID-19 vaccine delivery and essential immunization, Lessons learned for successful transition
  - Severity of disease associated with Omicron variant as compared with Delta variant in hospitalised patients with suspected or confirmed SARS-CoV-2 infection

- U.S. FDA[5] has issued press releases on:
  - On 17 June, FDA authorized Moderna and Pfizer-BioNTech COVID-19 vaccines for children down to 6 months of age
  - As of 21 June, 438 tests and sample collection devices are authorised by the FDA under emergency use authorisations (EUAs)

- ECDC[6] has issued new resources on:
  - Survey on the implementation of integrated surveillance of respiratory viruses with pandemic potential
  - Communicable disease threats report, 12-18 June 2022, week 24
  - Technical guidance for antigenic SARS-CoV-2 monitoring

- UKHSA[7] has issued new guidance and press releases on:
  - Highest-risk patients eligible for COVID-19 treatments: guide for patients
  - Reducing the spread of respiratory infections, including COVID-19, in the workplace

C. Scientific updates

Basic Science

- This longitudinal serological study in the United States evaluated the magnitude and potency of the endogenous antibody response to COVID-19 vaccination in participants who first received bamlanivimab in a prevention study (NCT04497987). The authors assessed the immune response to vaccination for 135 participants without prior SARS-CoV-2 infection who received either bamlanivimab (4200 mg) or placebo (day 1). All bamlanivimab and placebo recipients mounted a robust immune response to full COVID-19 vaccination, irrespective of age, risk-category, and vaccine type with any observed differences of uncertain clinical importance. These findings suggest that the benefit of

[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

receiving COVID-19 vaccination at the earliest opportunity outweighs the minimal effect on the endogenous immune response due to prior prophylactic COVID-19 monoclonal antibody infusion.

- This modelling study in China evaluated the link between genetic mismatch of circulating SARS-CoV-2 viruses and reported COVID-19 vaccine efficacy or effectiveness (VE) from population studies. The study was based on 78 VE data from 49 studies and 1,984,241 SARS-CoV-2 sequences collected from 31 regions. They found that genetic distance (GD) of the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein is highly predictive of vaccine protection and accounted for 86.3% (p= 0.038) of the VE change in a vaccine platform-based mixed-effects model and 87.9% (p= 0.006) in a manufacturer-based model. They applied the VE-GD model to predict protection mediated by existing vaccines against new genetic variants and validated the results by published real-world and clinical trial data, finding high concordance of predicted VE with observed VE. Estimated VE against the Delta variant was found to be 82.8% (95% CI: 68.7–96.0) using the mRNA vaccine platform, closely matching the reported VE of 83.0% from an observational study. Among the four sub-lineages of Omicron, the predicted VE varied between 11.9% and 33.3%, with the highest VE predicted against BA.1 and the lowest against BA.2, using the mRNA vaccine platform.
- This study in the United Kingdom assessed T and B cell immunity against B.1.1.529 (Omicron) in 731 triple mRNA vaccinated healthcare workers (HCWs) with different SARS-CoV-2 infection histories. B and T cell immunity against previous variants of concern was enhanced in triple vaccinated individuals, but magnitude of T and B cell responses against B.1.1.529 spike protein was reduced. Immune imprinting by infection with the earlier B.1.1.7 (Alpha) variant resulted in less durable binding antibody against B.1.1.529. Previously infection-naïve HCW who became infected during the B.1.1.529 wave showed enhanced immunity against earlier variants, but reduced neutralising antibody potency and T cell responses against B.1.1.529 itself. Previous Wuhan Hu-1 infection abrogated T cell recognition and any enhanced cross-reactive neutralising immunity on infection with B.1.1.529.

Vaccines

- This national, matched, test-negative, case–control study in Qatar assessed the effectiveness of vaccination with BNT162b2 or mRNA-1273, natural immunity due to previous infection with variants other than omicron, and hybrid immunity against symptomatic omicron infection and against severe, critical, or fatal COVID-19. The effectiveness of previous infection alone against symptomatic BA.2 infection was 46.1% (95% CI, 39.5 to 51.9). The effectiveness of vaccination with 2 doses of BNT162b2 and no previous infection was negligible (−1.1%; 95% CI, −7.1 to 4.6), but nearly all persons had received their second dose more than 6 months earlier. The effectiveness of 3 doses of BNT162b2 and no previous infection was 52.2% (95% CI, 48.1 to 55.9). The effectiveness of previous infection and 2 doses of BNT162b2 was 55.1% (95% CI, 50.9 to 58.9), and the effectiveness of previous infection and 3 doses of BNT162b2 was 77.3% (95% CI, 72.4 to 81.4). Previous infection alone, BNT162b2 vaccination alone, and hybrid immunity all showed strong effectiveness (>70%) against severe, critical, or fatal COVID-19 due to BA.2 infection. The authors observed similar results for effectiveness against BA.1 infection and of vaccination with mRNA-1273.
- This test-negative case-control study in the United States assessed the effectiveness of maternal vaccination against hospitalisation for COVID-19 among infants younger than 6 months of age. The study involved 537 case infants (with COVID-19) and 512 control infants (without COVID-19) across 30 hospitals in 22 states. Proportions of infants born to mothers who had been fully vaccinated against COVID-19 during pregnancy were 16% and 29% in the cases and controls respectively. Among the case infants, 113 (21%) received intensive care (64 [12%] received mechanical ventilation or vasoactive infusions). Two case infants died from COVID-19; neither infant's mother had been vaccinated during pregnancy. The effectiveness of maternal vaccination against hospitalisation for COVID-19 among infants was 52% (95% CI, 33 to 65) overall, 80% (95% CI, 60 to 90) during the delta period, and 38% (95% CI, 8 to 58) during the omicron period. Effectiveness was 69% (95% CI, 50 to 80) when maternal vaccination occurred after 20 weeks of pregnancy and 38% (95% CI, 3 to 60) during the first 20 weeks of pregnancy. These findings provide additional support for the current recommendations regarding COVID-19 vaccination during pregnancy.

- This randomised, placebo-controlled, phase 2, clinical trial in Cuba assessed the response of memory B cells after a single dose of the FINLAY-FR-1A vaccine in individuals with past SARS-CoV-2 infection. The study involved 450 convalescent participants with a history of asymptomatic, mild, or moderate COVID-19. Twenty (20) participants aged 60–78 years were included in the open, single-group, phase 2a study and 430 participants were randomly assigned to the experimental (n=344) or control groups (n=86) in the phase 2b study of participants aged 19–78 years. In the phase 2a volunteers 19/20 (95%) achieved a successful immune response after vaccination. No vaccine-associated serious adverse events were reported in the whole study population. Minor adverse events were found, the most common being pain at the injection site (105/364 [29%] in the intervention group; and 13/86 [15%] in the placebo group). A successful immune response was found in 289/358 (81%) of participants 28 days after vaccination. The vaccine elicited a greater than 31-times increase in anti-RBD-IgG antibodies compared with pre-vaccination rates, and the seroconversion rate was 302/358 (84%) on day 28 after vaccination; the geometric mean titres of live-virus neutralisation test increased from 15.4 (95% CI 10.3–23.2) to 400.3 (272.4–588.1) and high response was found against alpha, beta, and delta variants of concern.
- This phase 2/3 open-label, non-randomised, multicentre study in India assessed the safety and immunogenicity of BBV152 in children aged 2–18 years. The study enrolled 526 children across 6 hospitals, sequentially into groups 1 (n=176), 2 (n=175), and 3 (n=175). The vaccine was well tolerated with no serious adverse events, deaths, or withdrawals due to an adverse event reported during the study. Geometric mean titres (GMTs) of microneutralization antibodies at day 56 in groups 1 (138.8 [95% CI 111.0–173.6]), 2 (137.4 [99.1–167.5]), and 3 (197.6 [176.4–221.4]) were similar to titres in vaccinated adults (160.1 [135.8–188.8]) and with Biodefense and Emerging Infections, Research Resources Repository (BEI) reference serum samples (103.3 [50.3–202.1]). Similar results were obtained using the plaque reduction neutralisation test (PRNT), in which 166 (95%) of 175 participants in group 1, 165 (98%) of 168 in group 2, and 169 (98%) of 172 in group 3 seroconverted at day 56. The GMT ratio of PRNT titres in children and adults was 1.76 (95% CI 1.32–2.33), indicating a superior response in children compared with adults.
- This prospective cohort study in Germany assessed the humoral and cellular immune response after administering a third vaccine dose in patients with immune mediated inflammatory diseases (IMID). The study involved 66 IMID patients (33 treated with rituximab [RTX]) who did not respond to 2 doses of the SARS-CoV-2 vaccine. Patients received either BNT162b2 or ChAdOx1 nCoV-19 vaccine. Overall, 49.2% patients seroconverted and 50.0% developed neutralising antibody activity. Seroconversion (78.8% vs 18.2%) and neutralising activity (80.0% vs 21.9%) was higher in non-RTX than RTX-treated patients with IMID, respectively. Humoral vaccination responses were not different among patients showing positive (59.3%) or negative (49.7%) T cell responses at baseline. Patients remaining on mRNA-based vaccines showed similar vaccination responses compared with those switching to vector-based vaccines. These findings suggest that fast SARS-CoV-2 revaccination should be considered in patients with IMID that did not achieve protective immunity after two SARS-CoV-2 vaccinations.
- This test negative case-control study in Brazil assessed the change in odds of COVID-19 over time following primary series completion of the inactivated whole virus vaccine CoronaVac (Sinovac Biotech). The study involved 52,170 cases with symptomatic COVID-19 and 69,115 controls. Adjusted odds ratios of symptomatic COVID-19 increased with time since completion of the vaccination series. The increase in odds was greater in younger people and among healthcare workers. The adjusted odds ratios of COVID-19 related hospital admission or death significantly increased with time compared with the odds 14-41 days after series completion: from 1.25 (95% CI: 1.04 to 1.51) at 70-97 days up to 1.94 (1.41 to 2.67) from 182 days onwards. These findings provide supportive evidence for the implementation of vaccine boosters in these populations who received this inactivated vaccine.
- This single-centre case series in the United States assessed the frequency and outcomes of breast imaging-identified ipsilateral axillary lymphadenopathy (IAL) after recent COVID-19 vaccination. The authors found that 3,008/15,465 (19%) patients who underwent imaging had received recent COVID-19 vaccinations. Of 3,008 women, 308 (10%) had postvaccination IAL detected on screening mammograms, diagnostic mammograms or magnetic resonance imaging scan. The frequency of IAL

detections by vaccine manufacturer was 9% (172/1,836) for BioNTech-Pfizer, 12% (126/1,045) for Moderna, and 5% (7/127) for Johnson & Johnson. Of 47 patients with IAL undergoing ultrasonography, 62% had complete IAL resolution, including 22 patients with risk factors. Of patients without risk factors, very few (13/308 [4%]) had persistent symptoms requiring ultrasonography or biopsy. Of all patients, including those eventually undergoing biopsy (13/308 [4%]), none had malignant neoplasms. The authors recommend further multi-institutional assessments to clarify the patterns and outcomes of postvaccination IAL.

- This self-controlled case series in Norway, Finland and Denmark evaluated the association between AZD1222, BNT162b2, and mRNA-1273 vaccines and subsequent thromboembolic and thrombocytopenic events. The study involved 265,339 individuals with hospital contacts because of coronary artery disease, coagulation disorders, or cerebrovascular disease between 1 January 2020, and 16 May 2021. There was an increased rate of hospital contacts because of coagulation disorders and cerebrovascular disease, especially for thrombocytopenia (RR: 4.29 [95% CI, 2.96-6.20]) and cerebral venous thrombosis (RR:12.04 [95% CI, 5.37-26.99]), following vaccination with AZD1222. Although increased rates of several thromboembolic and thrombocytopenic outcomes following BNT162b2 and mRNA-1273 vaccination were observed, these increases were less than the rates observed after AZD1222, and sensitivity analyses were not consistent. The authors recommend confirmatory analysis on the 2 mRNA vaccines by other methods.
- This randomised trial in the United States assessed whether text messaging with behavioural insights would increase participation in COVID-19 vaccine uptake. The study involved 16,045 adults randomly assigned in a 1:20:20 ratio to (1) outbound telephone call only by call centre, (2) text message and outbound telephone call by call centre to those who respond, or (3) text message, with patients instructed to make an inbound telephone call to a hotline. At 1 month, 14/390 patients (3.6% [95% CI, 1.7%-5.4%]) in the outbound telephone call–only group completed 1 vaccine dose, as did 243/7890 patients (3.1% [95% CI, 2.7%-3.5%]) in the text plus outbound call group (absolute difference, −0.5% [95% CI, −2.4% to 1.4%]; p = 0.57) and 253/7765 patients (3.3% [95% CI, 2.9%-3.7%]) in the text plus inbound call group (absolute difference, −0.3% [95% CI, −2.2% to 1.6%]; p = 0.72). Among the 15,655 patients receiving text messaging, 118/3,889 patients (3.0% [95% CI, 2.5%-3.6%]) in the standard messaging group completed 1 vaccine dose, as did 135/3920 patients (3.4% [95% CI, 2.9%-4.0%]) in the clinician endorsement group (absolute difference, 0.4% [95% CI, −0.4% to 1.2%]; p = 0.31), 100 /3911 patients (2.6% [95% CI, 2.1%-3.1%]) in the scarcity group (absolute difference, −0.5% [95% CI, −1.2% to 0.3%]; p= 0.20), and 143/3935 patients (3.6% [95% CI, 3.0%-4.2%]) in the endowment group (absolute difference, 0.6% [95% CI, −0.2% to 1.4%]; p = 0.14). Text messaging offers a low-cost alternative to outbound telephone calls, but additional efforts are needed to increase vaccine uptake.

Diagnostics

- This study in Germany describes the development of a multiplexed proteomics assay for determining disease severity and prognosis in COVID-19. The assay quantifies up to 50 peptides, derived from 30 known and newly introduced COVID-19-related protein markers, in a single measurement using routine-lab compatible analytical flow rate liquid chromatography and multiple reaction monitoring (LC-MRM). The assay was validated in 2 observational studies in Germany before and after dexamethasone became standard of care. The assay produces reproducible (median inter-batch CV of 10.9%) absolute quantification of 47 peptides with high sensitivity (median LLOQ of 143 ng/ml) and accuracy (median 96.8%). In both studies, the assay reproducibly captured hallmarks of COVID-19 infection and severity, as it distinguished healthy individuals, mild, moderate, and severe COVID-19. In the post-dexamethasone cohort, the assay predicted survival with an accuracy of 0.83 (108/130), and death with an accuracy of 0.76 (26/34) in the median 2.5 weeks before the outcome, thereby outperforming compound clinical risk assessments such as SOFA, APACHE II, and ABCS scores.
- This case series in the United States evaluated the performance of rapid antigen tests (RATs) in detecting SARS-CoV-2 in the context of a dominant Omicron variant. The study included 723 university students aged 17 to 23 years who self-administered a RAT (BinaxNOW; Abbott Laboratories) within 24 hours of campus arrival. Asymptomatic students with a positive RAT result underwent RT-PCR

testing. Forty-six participants (6.4%) had positive RAT findings, of whom 35 (76.1%) had symptomatic infections. Overall, RAT had a sensitivity of 63.0% (95% CI, 51.9%-74.1% [46 of 73]) and specificity of 99.8% (95% CI, 99.5%-100% [1 of 650]). Among symptomatic participants, RAT had a sensitivity of 77.8% (95% CI, 65.6%-89.9% [35 of 45]); among asymptomatic patients, 39.2% (95% CI, 21.2%-57.4% [11 of 28]). Participants with RAT- and RT-PCR–positive findings (n = 23) had a lower median Ct value of 24.6 (IQR, 22.2-32.3) compared with those with RAT-negative and RT-PCR–positive findings (n = 27), with a median Ct value of 35.0 (IQR, 29.8-36.6; p < 0.001). In the RT-PCR–positive cohort, symptomatic individuals (n = 22) had lower Ct values compared with their asymptomatic counterparts (24.7 [IQR, 22.4-31.9] vs 33.6 [IQR, 29.3-35.7]; p = 0.004).

Care and Treatment

- This multicentre, randomised trial in the United Kingdom evaluated the non-inferiority of high-flow nasal cannula therapy (HFNC) as the first-line mode of non-invasive respiratory support for acute illness, compared with continuous positive airway pressure (CPAP), for time to liberation from all forms of respiratory support. The study involved 573 acutely ill children aged <15 years across 24 critical care units. Patients were randomised 1:1 to commence either HFNC at a flow rate based on patient weight or CPAP of 7 to 8 cm H_2O. The median time to liberation in the HFNC group was 52.9 hours (95% CI, 46.0-60.9 hours) vs 47.9 hours (95% CI, 40.5-55.7 hours) in the CPAP group (absolute difference, 5.0 hours [95% CI –10.1 to 17.4 hours]; adjusted hazard ratio 1.03 [1-sided 97.5% CI, 0.86-∞]). This met the criterion for non-inferiority. Of the 7 prespecified secondary outcomes, 3 were significantly lower in the HFNC group: use of sedation (27.7% vs 37%; adjusted OR, 0.59 [95% CI, 0.39-0.88]); mean duration of critical care stay (5 days vs 7.4 days; adjusted mean difference, −3 days [95% CI, −5.1 to −1 days]); and mean duration of acute hospital stay (13.8 days vs 19.5 days; adjusted mean difference, −7.6 days [95% CI, −13.2 to −1.9 days]). The most common adverse event was nasal trauma (HFNC: 6/295 [2.0%]; CPAP: 18/278 [6.5%]).

Epidemiology

- This cross-sectional study assessed the seropositivity of SARS-CoV-2 among healthcare workers (HCWs) and general population in Kita region of Mali. The study utilised 2,392 routine surveillance samples from 12 health facilities, 397 samples from 113 HCWs in 5 health facilities and community serosurvey in 16 villages in or near Kita town. From 2,392 routine surveillance samples, 68 (2.8%, 95% CI: 2.2% to 3.6%) tested positive for SARS-CoV-2 by RT-PCR. The monthly positivity rate was 0% in June-August 2020 and gradually increased to 6% by December 2020 and 6.2% by January 2021, then declined to 5.5%, 3.3%, 3.6% and 0.8% in February, March, April and May 2021, respectively. From 397 serum samples collected from 113 HCWs, 175 (44.1%, 95% CI: 39.1% to 49.1%) were positive for SARS-CoV-2 antibodies. The monthly seroprevalence was around 10% from September to November 2020 and increased to over 40% from December 2020 to May 2021. For community serosurvey in December 2020, overall seroprevalence of SARS-CoV-2 antibodies was 27.7%. The highest age-stratified seroprevalence was observed in participants aged 60-69 years (45.5%, 95% CI: 32.3% to 58.6%). The lowest was in children aged 0-9 years (14.0%, 95% CI: 7.4% to 20.6%). SARS-CoV-2 in rural Mali is much more widespread than assumed by national testing data and particularly in the older population and frontline HCWs.
- This multi-centre cohort study in Kenya assessed outcomes of patients admitted to hospital with COVID--19 and determined the predictors of mortality. The study involved 787 patients with RT-PCR confirmed SARS-CoV-2 infection across 6 facilities. At admission, 455 (58%) were symptomatic with an additional 63 (9%) developing clinical symptoms during hospitalisation. The most common symptoms were cough (337, 43%), loss of taste or smell (279, 35%) and fever (126, 16%). Comorbidities were reported in 340 (43%), with cardiovascular disease, diabetes and HIV documented in 130 (17%), 116 (15%), 53 (7%), respectively. 90 (11%) were admitted to the Intensive Care Unit (ICU) for a mean of 11 days, 52 (7%) were ventilated with a mean of 10 days, 107 (14%) died. The risk of death increased with age (HR 1.57 (95% CI 1.13 to 2.19)) for persons >60 years compared with

those <60 years old; having comorbidities (HR 2.34 (1.68 to 3.25)) and among men (HR 1.76 (1.27 to 2.44)) compared with women. Elevated white cell count and aspartate aminotransferase were associated with higher risk of death.

- This systematic review and meta-analysis of 88 studies aimed to estimate the prevalence of global SARS-CoV-2 serology in different populations and geographical areas. A total of 414,773 serological tests were performed in all studies. The results showed that SARS-CoV-2 seroprevalence is between 3 and 15% worldwide. In the Eastern Mediterranean region, the pooled estimate of seroprevalence SARS-CoV-2 was 15% (CI 95% 5–29%), and in Africa, the pooled estimate was 6% (CI 95% 1–13%). In America, the pooled estimate was 8% (CI 95% 6–11%), and in Europe, the pooled estimate was 5% (CI 95% 4–6%). The pooled estimate was 3% (CI 95% 2–4%) in Western Pacific. The authors also analysed three of these areas separately. The analysis estimated the prevalence in subgroups such as study population, diagnostic methods, sampling methods, time, perspective, and type of the study. Countries need to implement prevention policies with greater sensitivity and follow-up, especially those with low COVID-19 serology prevalence and vaccination coverage.
- This case series in Belgium reports on the co-identification of SARS-CoV-2 variants B.1.1.529 (Omicron) and B.1.617.2 (Delta) in two geographically unrelated cases. The 1st case is a man aged 38 years who presented himself to a general practitioner in Anderlecht on 23 December 2021 with a congested nose, sore throat, and fatigue. The 2nd case is a 34-year-old woman from Brussels who presented to the emergency unit of a hospital with history of fever, muscle aches and shortness of breath. The co-infections were detected simultaneously using the Oxford Nanopore Technologies (ONT) GridION. Two main arguments that support the co-infection events: (1) the total number of reads supporting each variant was high (around 1.78 million reads mapping to Omicron vs 218 thousand reads mapping to Delta for case 1; and 4.17 million reads to Omicron vs 708 thousand reads mapping to Delta for case 2), and (2) sampling and PCR diagnostic tests of samples were performed at different moments and in different laboratories. These findings highlight the importance of genomic surveillance to diagnose SARS-CoV-2 co-infection with different variants and emphasize that more needs to be learned about these co-infection events and their influence on COVID-19 outcome and vaccine efficacy.

Infection Prevention & Control

- This ongoing, phase 3 trial assessed the effectiveness of AZD7442 (tixagevimab and cligavimab) for the prevention of symptomatic and severe COVID-19 in adults (≥18 years of age). The study involved 5,197 participants across 87 sites in Belgium, France, Spain, the United Kingdom, and the United States. Participants were randomised (2:1) to receive one dose of AZD7442 or placebo. In total, 1221/3,461 participants (35.3%) in the AZD7442 group and 593/1,736 participants (34.2%) in the placebo group reported having at least one adverse event, most of which were mild or moderate in severity. Symptomatic COVID-19 occurred in 8/3,441 participants (0.2%) in the AZD7442 group and in 17 of 1731 participants (1.0%) in the placebo group (relative risk reduction, 76.7%; 95% CI, 46.0 to 90.0; p<0.001). Extended follow-up at a median of 6 months showed a relative risk reduction of 82.8% (95% CI, 65.8 to 91.4). Five cases of severe or critical COVID-19 and two COVID-19–related deaths occurred, all in the placebo group.

Non-pharmaceutical interventions, social distancing

- This modelling study in India aimed to assess the timing, composition, and intensity of public health interventions (PHIs) that, if applied nationally, might have blunted the sharp rise of the second wave. The authors produce evidence in support of how strengthening public health interventions early would have helped control transmission in the country and significantly reduced mortality during the second wave, even without harsh lockdowns. They found that enhanced surveillance at district, state, and national levels and constant assessment of risk associated with increased transmission are critical for future pandemic responsiveness. They propose a tiered intervention framework aimed at curbing future

COVID-19 waves arising from highly transmissible emerging variants that could have immune escape properties in populations where vaccination rates remain suboptimal.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 17 June 2022, Pfizer and BioNTech announced the U.S. Food and Drug Administration (FDA) granted emergency use authorization (EUA) of the Pfizer-BioNTech COVID-19 Vaccine as a three 3-µg dose series for children 6 months through 4 years of age. The EUA is based on data from a Phase 2/3 randomised, controlled trial that included 4,526 children 6 months through 4 years of age. In the trial, the SARS-CoV-2-neutralising antibody geometric mean titre (GMT) one month after the third dose was 1,535.2 (95% CI, 1,388.2, 1,697.8) in children 2 through 4 years of age and 1,406.5 (95% CI, 1,211.3, 1,633.1) in infants 6 through 23 months. The antibody responses in both age groups were comparable to those recorded in people 16 to 25 years of age immunized with two 30-µg doses and met the pre-specified success criteria to declare non-inferiority. Three 3-µg doses of the Pfizer-BioNTech COVID-19 Vaccine demonstrated a favourable safety and tolerability profile comparable to placebo. Clinical trial registration #: (NCT04816643).
- On 17 June 2022, Bharat Biotech announced that BBV152 (COVAXIN), a whole-virion inactivated COVID-19 vaccine candidate, has proven to be safe, well-tolerated, and highly immunogenic in paediatric subjects in phase 2/3 study. The Phase 2/3 study is an open-label, and multicentre to evaluate the safety, reactogenicity, and immunogenicity of COVAXIN in healthy children and adolescents in 2-18 years of age group. In the trial COVAXIN demonstrated safety, less reactogenic, and robust immunogenicity. Clinical trial registration #: (NCT04918797).
- On 15 June 2022, Pfizer and BioNTech announced the European Medicines Agency (EMA) has initiated a rolling review for a variant-adapted version of the Pfizer COVID-19 vaccine. This rolling review is initially based on chemistry, manufacturing, and controls (CMC) data shared with EMA. As clinical data become available, including data on immunogenicity against Omicron and its subvariants, it will be added to the rolling submission. Pfizer and BioNTech are evaluating several variant-adapted vaccines.
- On 13 June 2022, Novavax announced the Australian Therapeutic Goods Administration (TGA) has granted provisional registration of Nuvaxovid (NVX-CoV2373) COVID-19 vaccine as a booster in individuals aged 18 and over. The provisional registration was based on data from Novavax' Phase 2 trial conducted in Australia, from a separate Phase 2 trial conducted in South Africa, and from the UK-sponsored COV-BOOST trial. As part of the Phase 2 trials, a single booster dose of Nuvaxovid was administered to healthy adult participants approximately six months after their primary two-dose vaccination series of Nuvaxovid. The third dose produced increased immune responses comparable to or exceeding levels associated with protection in Phase 3 clinical trials. In the COV-BOOST trial, Nuvaxovid induced a robust antibody response when used as a heterologous third booster dose. Local and systemic reactions observed were generally short-lived with a median duration of approximately two days following the booster. Safety reporting of reactogenicity events showed an increasing incidence across all three doses of Nuvaxovid, reflecting the increased immunogenicity seen with a third dose. Clinical trial registration #: (NCT04611802).
- On 13 June 2022, Sanofi reports data from two trials, VAT02 Cohort 2 and COVIBOOST VAT013, conducted with the COVID-19 booster vaccine candidate modelled on the Beta variant antigen. In the Phase 3 VAT02 Cohort 2 study, the vaccine candidate induced (at day 15 post-immunization) a significant boost in antibody titres above baseline against multiple variants of concern (15-fold increase against D614 parent virus, 30-fold increase against Beta strain) in adults previously primed with mRNA COVID-19 vaccines. In particular, against Omicron, preliminary data show a 40-fold increase against BA.1. The booster vaccine candidate generated double the number of neutralising antibodies against Omicron BA.1 and BA.2 compared to the D614-based (original parent virus) booster. The independent COVIBOOST (VAT013) study demonstrated that, following primary vaccination with two doses of Pfizer-BioNTech's Comirnaty vaccine, the booster vaccine candidate generated a higher immune response (as measured by neutralising antibody titres) than Pfizer-BioNTech's booster or the booster

vaccine candidate, both of which target the original D614 parent strain. Across both studies, the vaccine candidate was well-tolerated, with a favourable safety profile. In the VAT02 cohort 2 study, low numbers (less than 4%) of Grade 3 reactions were reported, all transient and non-severe. Clinical trial registration #: (NCT05405283 & NCT05124171).

- On 8 June 2022, Moderna announced new clinical data on its Omicron-containing bivalent COVID-19 booster candidate, mRNA-1273.214, containing mRNA-1273 (Spikevax) and a vaccine candidate targeting the Omicron variant of concern. In the phase 2/3 trial, mRNA-1273.214 met all primary endpoints including neutralising antibody response against Omicron when compared to a 50 µg booster dose of mRNA-1273 in baseline seronegative participants. Pre-specified criteria for superiority as measured by neutralising geometric mean titre ratio (GMR) with the lower bound of the confidence interval >1 was met. The GMR and corresponding 97.5% confidence interval was 1.75 (1.49, 2.04). A booster dose of mRNA-1273.214 increased neutralising geometric mean titres (GMT) against Omicron approximately 8-fold above baseline levels. Primary endpoints of non-inferiority against ancestral SARS-CoV-2 were also met, with GMR against ancestral SAR-COV-2 (D614G) of 1.22 (1.08-1.37). The booster dose of mRNA-1273.214 was generally well-tolerated, with side effects comparable to a booster dose of mRNA-1273 at the 50µg dose level. Clinical trial registration #: (NCT05249829).

Therapeutics trials:

- On 20 June 2022, Kinarus Therapeutics announced KIN001's strong antiviral efficacy against the original SARS-CoV-2 strain and variants of concern (VOC). KIN001's effects fight SARS-CoV-2 in three complementary ways: anti-viral effects may prevent viral replication; anti-inflammatory effects may reduce the body's inappropriate inflammatory response (e.g. "cytokine storm"); anti-fibrotic effects may enhance healing of damaged tissues, speeding recovery and reducing the likelihood of "long COVID" symptoms. In contrast to vaccines, antibody, and nucleic acid-based therapies which target viral proteins, KIN001 targets host cell pathways essential for viral replication. This mechanistic difference is less likely to be evaded by future VOCs which result from mutations in SARS-CoV-2 virus. The first Phase 2 clinical trial of KIN001 to treat hospitalised COVID-19 patients ("KINETIC") had enrolled 130 patients. Results showed KIN001 almost completely blocked virus replication in multiple human cell lines for all SARS-CoV-2 strains, including VOC, like the highly infectious delta and omicron variants. This indicate that KIN001 may be an effective therapy for the treatment of SARS-CoV-2 infection for present and potential future variants.
- On 16 June 2022, Moleculin Biotech reported preliminary results from the first cohort of the first-in-human Phase 1a study of WP1122. WP1122 was developed as a 2-deoxy-D-glucose (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 tumour 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 is a first-in-human, randomised, double-blind, placebo-controlled, overlapping single ascending doses (SAD) and multiple ascending doses (MAD) to investigate the effects of WP1122 administered as an oral solution in healthy human volunteers. The 1st cohort consisted of 9 subjects dosed with 8 mg/kg or placebo in the dose escalation trial evaluating the safety and pharmacokinetics (PK) of WP1122 in healthy volunteers in the United Kingdom (UK). Based on the overall results in this Cohort that deemed safe and well-tolerated, the SAD Cohort 2 with a dose escalation to 16 mg/kg began. Dose escalation will take place in sequential SAD cohorts, and MAD will start as soon as SAD has successfully completed at least 3 dosing cohorts. Clinical trial registration #: (NCT05195723).
- On 14 June 2022, PureTech Health announced results from a Phase 2 study of LYT-100-COV (deupirfenidone) in patients with post-acute "Long" COVID with respiratory complications. LYT-100 is a selectively deuterated form of pirfenidone that is designed to retain the potent and clinically-validated anti-fibrotic and anti-inflammatory activity of pirfenidone. It is being advanced for the potential treatment of conditions involving inflammation and fibrosis, including idiopathic pulmonary fibrosis and breast cancer-related, upper limb secondary lymphedema. The global, double-blind, randomised, placebo-controlled phase 2 study is one of few to complete in patients with post-acute COVID. The study enrolled 177 patients averaging 55 years of age who experienced continued respiratory complications

following hospitalisation for acute COVID-19 infection that required treatment with supplemental oxygen. The primary efficacy endpoint was a three-month change from baseline compared to placebo on the six-minute walk test (6MWT) distance. The 6MWT determines how far a patient can walk in six minutes and is a commonly used measure of functional capacity in a variety of cardio-pulmonary diseases. Individuals in both the treatment and placebo arms meaningfully improved walking distance on the 6MWT as compared to baseline, and no statistically significant differences between treatment groups were observed. There was no treatment effect observed in this indication with LYT-100, though the strong safety and tolerability profile of LYT-100 seen in previous studies was reaffirmed. Clinical trial registration #: (NCT04652518).

Immunotherapies trials:

- On 9 June 2022, Immunome announced the first patient has been enrolled in a clinical trial of IMM-BCP-01, a three-antibody cocktail for the treatment of SARS-CoV-2 (COVID-19). IMM-BCP-01 is a three-antibody cocktail targeting non-overlapping regions of the Spike protein of SARS-CoV-2, including highly conserved, subdominant epitopes, which elicits both ACE2 and non-ACE2 dependent neutralisation, and induces natural viral clearance mechanisms, such as antibody dependent cellular cytotoxicity, complement activation and phagocytosis. The Phase 1b study of IMM-BCP-01 is a single dose, dose escalation study in recently diagnosed COVID-19 patients. The primary study endpoint is safety, with pharmacokinetics (PK) and virology as secondary assessments.
- On 9 June 2022, Brii Biosciences announced positive data from a randomised, single-blind clinical study of its long-acting COVID-19 neutralising antibody therapy, the amubarvimab/ romlusevimab combination, in China. The clinical trial of the amubarvimab/ romlusevimab combination to evaluate the safety, tolerability, and preliminary clinical efficacy of the combination treatment in 48 people infected with SARS-CoV-2 (virus that causes COVID-19) was conducted in China. The results of the study shows that the amubarvimab/ romlusevimab combination was generally safe and well-tolerated in both severe and non-severe SARS-CoV-2 infected subjects. All eight subjects with severe SARS-CoV-2 infections treated with the combination therapy had their viral loads significantly reduced from baseline levels with no subjects experiencing exacerbations that required mechanical ventilation or led to death. Among the 40 subjects with non-severe SARS-CoV-2 infections treated with the combination therapy had several clinical benefits observed, including RNA conversion rate (93% in treatment arm vs. 64% in placebo arm), median time to symptom resolution (8 days in treatment arm vs. 10 days in placebo arm), and proportion of progression to severe cases (0% in treatment arm vs. 5% in placebo arm). These findings are consistent with the results of the global ACTIV-2 Phase 3 trial conducted in 837 subjects. Clinical trial registration #: (NCT04787211).
- On 7 June 2022, Tevogen Bio announced it has initiated the fourth and final dose level of its investigational T cell therapy for high-risk COVID-19 patients. The open-label clinical trial is designed to study the safety and optimal dose of its investigational target-specific T cell therapy when given to high-risk COVID-19 patients (age ≥ 18 years with predefined high-risk criteria) or those who are 65 or older (with or without previously identified comorbid conditions). Participants receiving the investigational therapy will be compared to patients receiving standard of care within the context of the study. Each patient in the third cohort received a single infusion (1 x 106cells/kg) of TVGN-489, a higher dosing level than the first (1 x 105cells/kg) and second cohorts (3 x 105 cells/kg). No dose limiting toxicities or treatment-related adverse events, including Cytokine Release Syndrome (CRS), have been observed to date in any of the cohorts. In addition, as a secondary outcome measure, all patients in the three cohorts experienced a correction of lymphopenia, which is the rapid return to baseline in lymphocyte levels. Clinical trial registration #: (NCT04765449).

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