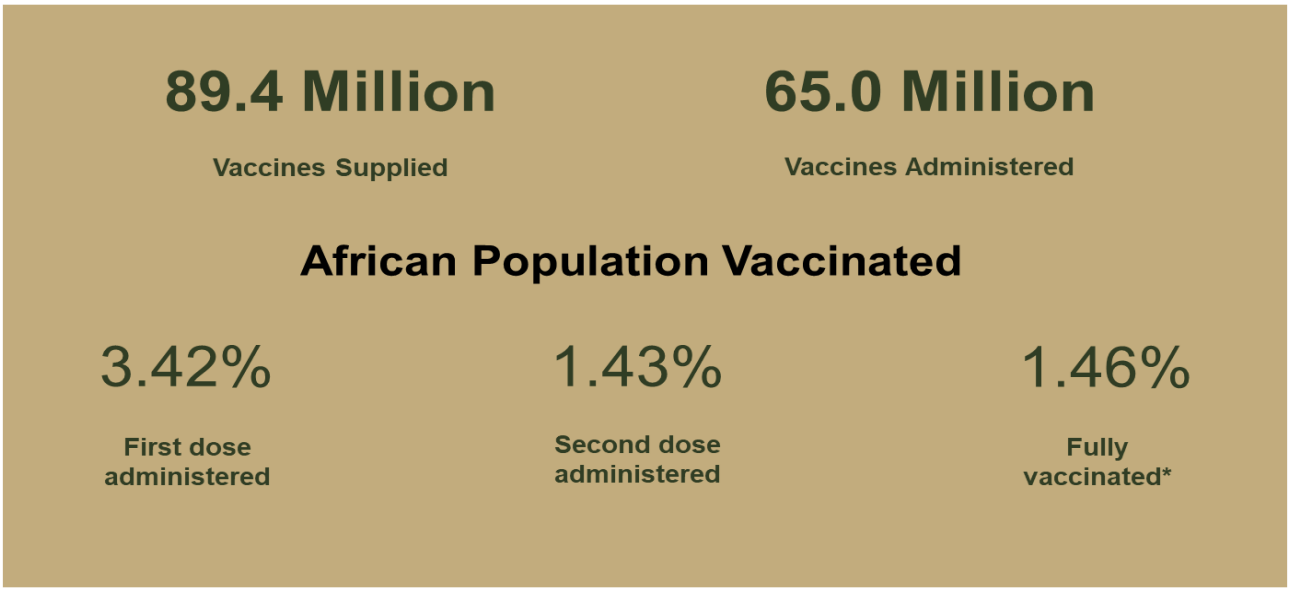
COVID-19 Scientific and Public Health Policy Update[1] – (03 August 2021)

In addition to the Weekly Outbreak Brief and other documents on the spread of COVID-19 and the actions that the African Union/Africa CDC and WHO/AFRO are taking to help African Union Member States, we share a biweekly brief detailing the latest developments in scientific knowledge and public health policy from around the world, as well as updates to the latest guidance from Africa CDC, WHO and other public health agencies. Contents of this document are ***not intended to serve as recommendations*** *from the African Union-Africa CDC or WHO/AFRO; rather, it is a summary of the scientific information available in the public space to Member States. It is important to note that the outbreak is evolving rapidly and that 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 in these areas.*

A. Trending Topics

Status of Vaccines in Africa

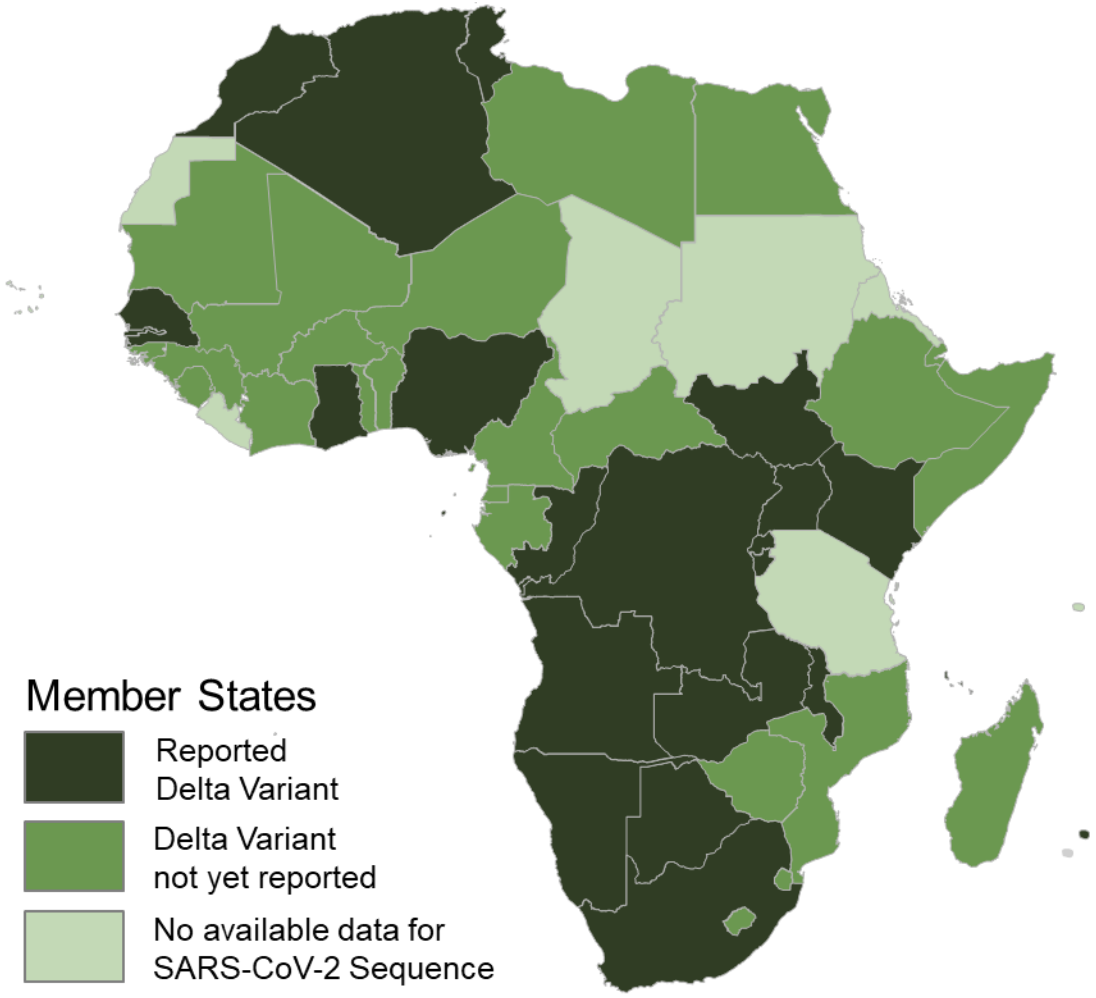


*Received two doses/ one dose of Johnson & Johnson vaccine
https://africacdc.org/covid-19-vaccination/
Updated 28th July 2021

Variants of Concern

- The B.1.617.2 (Delta variant), first reported in India, has spread to more than 182 countries worldwide; 21 Member States in Africa have reported this variant. https://africacdc.org/institutes/africa-pathogen-genomics-initiative/

[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 not considered policy, guidance, or final conclusions of the African Union- Africa CDC or WHO/AFRO**.



Updated 28th July 2021

B. New guidelines and resources

Since 17th July 2021,

- Africa CDC has published new guidance and resources on:
  - The Critical Role of Community Health Workers in COVID-19 Vaccine Roll Out
  - Statement on the remarkable progress made by several African countries as part of the Partnerships for African Vaccine Manufacturing (PAVM)
- US CDC has published new guidance and resources on:
  - Interim Public Health Recommendations for Fully Vaccinated People
  - Guidance for Institutions of Higher Education (IHEs)
  - Guidance for General Laboratory Safety Practices during the COVID-19 Pandemic
- WHO has published new guidance and resources on:
  - Interim recommendations for use of the ChAdOx1-S [recombinant] vaccine against COVID-19 (AstraZeneca COVID-19 vaccine AZD1222 Vaxzevria™, SII COVISHIELD™)
  - Annexes to the interim recommendations for use of the ChAdOx1-S [recombinant] vaccine against COVID-19
  - Health financing for the COVID-19 response: Process guide for national budgetary dialogue

- Guidance on conducting vaccine effectiveness evaluations in the setting of new SARS-CoV-2 variants: Interim guidance, 22 July 2021. Addendum to Evaluation of COVID-19 vaccine effectiveness
- Guidance on utilization of COVID-19 vaccines before the date of expiry
- Guidance for clinical case management of thrombosis with thrombocytopenia syndrome(TTS) following vaccination to prevent coronavirus disease (COVID-19)
- WHO SAGE Roadmap For Prioritizing Uses Of COVID-19 Vaccines In The Context Of Limited Supply

- FDA has issued press releases on:
  - FDA revised the Emergency Use Authorization (EUA) for REGEN-COV (casirivimab and imdevimab) to add an authorization for emergency use as post-exposure prophylaxis
  - FDA revised the EUA for baricitinib now authorizing baricitinib alone for the treatment of COVID-19 in hospitalized patients requiring supplemental oxygen
  - FDA authorized an extension for the shelf life of the refrigerated Janssen (Johnson & Johnson) COVID-19 Vaccine, allowing the product to be stored at 2-8 degrees Celsius for six months.
  - FDA issued an Emergency Use Authorization (EUA) to Becton, Dickinson and Company (BD) for its BD Vacutainer Plus Citrate Plasma Tubes
  - FDA posted frequently asked questions (FAQs) about sodium citrate blood specimen collection tubes.

- ECDC has issued new resources on:
  - Rapid Risk Assessment: COVID-19 outbreaks in long-term care facilities in the EU/EEA in the context of current vaccination coverage
  - Partial COVID-19 vaccination, vaccination following SARS-CoV-2 infection and heterologous vaccination schedule: summary of evidence

- PHE has issued new guidance and press releases on:
  - Guidance on equipment for temperature screening in the context of the COVID-19 pandemic
  - Technical specifications for personal protective equipment (PPE)
  - Guidance on the ventilation of indoor spaces to stop the spread of coronavirus (COVID-19)
  - Guidance for local authorities and local decision-makers on containing and managing COVID-19 outbreaks at a local level
  - Guidance for contacts of a person with a positive test result for coronavirus (COVID-19) who do not live with that person
  - Guidance for arranging or attending a funeral or commemorative event during the coronavirus (COVID-19) pandemic

The full list of latest guidance and resources from WHO and other public health institutions can be found in this link.

C. Scientific updates

Basic Science

- This study identified 27 genes related to inflammation and coagulation pathways whose genetically predicted expression was associated with COVID-19 hospitalisation. The authors integrated a genome-wide association study of COVID-19 hospitalisation (7,885 cases and 961,804 controls from COVID-19 Host Genetics Initiative) with mRNA expression, splicing, and protein levels (n = 18,502). They

functionally characterised the 27 genes using phenome- and laboratory-wide association scans in Vanderbilt Biobank (n = 85,460) and identified coagulation-related clinical symptoms, immunologic, and blood-cell-related biomarkers. They replicated their findings across trans-ethnic studies and observed consistent effects in individuals of diverse ancestral backgrounds in Vanderbilt Biobank, pan-UK Biobank, and Biobank Japan.

- This case series aimed to demonstrate the presence of presumed SARS-CoV-2 viral particles and its relevant proteins in the eyes of patients with COVID-19. The retina from enucleated eyes of 3 deceased patients with confirmed COVID-19 infection were submitted for immunofluorescence and transmission electron microscopy at a hospital in Brazil. Presumed S and N COVID-19 proteins were seen by immunofluorescence microscopy within endothelial cells close to the capillary flame and cells of the inner and the outer nuclear layers. At the perinuclear region of these cells, it was possible to observe by transmission electron microscopy double-membrane vacuoles that are consistent with the virus, presumably containing COVID-19 viral particles. Their findings suggest that the presumed SARS-CoV-2 viral particles may be involved in some of the infection's ocular clinical manifestations.
- This study used a longitudinal approach to describe the immune response to SARS-CoV-2 infection. The authors performed single-cell RNA sequencing of sequential bronchoalveolar lavage fluid cells obtained from SARS-CoV-2 infected ferrets. They compared these to negative controls at 2 days post infection (dpi) and 5 dpi. Their results provide fundamental information regarding the immune response dynamics provoked by SARS-CoV-2 infection, as well as a detailed description of the natural course and changes of macrophages in the ferret model.

Vaccines

- This test-negative case–control study in England aimed to estimate the effectiveness of vaccination against symptomatic disease caused by the delta variant or the predominant strain (B.1.1.7, or alpha variant) over the period that the delta variant began circulating. Effectiveness after one dose of vaccine (BNT162b2 or ChAdOx1 nCoV-19) was notably lower among persons with the delta variant (30.7%; 95% CI, 25.2 to 35.7) than among those with the alpha variant (48.7%; 95% CI, 45.5 to 51.7); the results were similar for both vaccines. With the BNT162b2 vaccine, the effectiveness of two doses was 93.7% (95% CI, 91.6 to 95.3) among persons with the alpha variant and 88.0% (95% CI, 85.3 to 90.1) among those with the delta variant. With the ChAdOx1 nCoV-19 vaccine, the effectiveness of two doses was 74.5% (95% CI, 68.4 to 79.4) among persons with the alpha variant and 67.0% (95% CI, 61.3 to 71.8) among those with the delta variant.
- This retrospective cohort study among 15,060 pregnant women in Israel aimed to assess the association between receipt of BNT162b2 mRNA vaccine and risk of SARS-CoV-2 infection. The cohort included 7530 vaccinated and 7530 matched unvaccinated women, 46% and 33% in the second and third trimester, respectively, with a mean age of 31.1 years (SD, 4.9 years). There were 118 SARS-CoV-2 infections in the vaccinated group and 202 in the unvaccinated group. Among infected women, 88 of 105 (83.8%) were symptomatic in the vaccinated group vs 149 of 179 (83.2%) in the unvaccinated group ($P \geq .99$). The hazards of infection were 0.33% vs 1.64% in the vaccinated and unvaccinated groups, respectively, with an adjusted hazard ratio of 0.22 (95% CI, 0.11-0.43). Vaccine-related adverse events were reported by 68 patients; none was severe. The most commonly reported symptoms were headache (n = 10), general weakness (n = 8), nonspecified pain (n = 6), and stomachache (n = 5).
- This randomised, single-center, open-label, phase 2 trial done in Zhongnan Hospital (Wuhan, China) aimed to evaluate the safety and immunogenecity of the Ad5-nCoV vaccine by aerosol inhalation in adults (≥18 years) seronegative for SARS-CoV-2. A total of 130 participants were enrolled into the trial and randomly assigned (1:1:1:1:1) into five groups to be vaccinated via intramuscular injection, aerosol

inhalation, or both. The authors report that the aerosolised Ad5-nCoV was well tolerated, and two doses of aerosolised Ad5-nCoV elicited neutralising antibody responses, similar to one dose of intramuscular injection. An aerosolised booster vaccination at 28 days after first intramuscular injection induced strong IgG and neutralising antibody responses. Their current data support the evaluation of aerosolised Ad5-nCoV in ongoing phase 2 and 3 clinical trials.

- This observational study aimed to assess the immunogenicity and reactogenicity of a heterologous vector/mRNA prime–booster regimen in comparison to the standard homologous regimens. A total of 216 immunocompetent individuals were prospectively enrolled before secondary vaccination with the authorized vaccines ChAdOx1 nCoV-19, BNT162b2 or mRNA-1273. The authors report that, in healthy adult individuals ($n = 96$), the heterologous vaccine regimen induced spike-specific IgG, neutralizing antibodies and spike-specific CD4 T cells, the levels of which were significantly higher than after homologous vector vaccine boost ($n = 55$) and higher or comparable in magnitude to homologous mRNA vaccine regimens ($n = 62$). Spike-specific CD8 T cell levels after heterologous vaccination were significantly higher than after both homologous regimens. Spike-specific T cells were predominantly polyfunctional with largely overlapping cytokine-producing phenotypes in all three regimens. Recipients of both the homologous vector regimen and the heterologous vector/mRNA combination reported greater reactogenicity following the priming vector vaccination, whereas heterologous boosting was well tolerated and comparable to homologous mRNA boosting.
- This study among fully vaccinated health care workers in Israel aimed to identify breakthrough infections that occurred. Among 11,453 fully vaccinated health care workers, 1497 (13.1%) underwent RT-PCR testing during the study period. Of the tested workers, 39 breakthrough cases were detected. The average age of the 39 infected workers was 42 years, and the majority were women (64%). The median interval from the second vaccine dose to SARS-CoV-2 detection was 39 days (range, 11 to 102). Only one infected person (3%) had immunosuppression. Most breakthrough cases were mild or asymptomatic. The most common symptom that was reported was upper respiratory congestion (36% of all cases), followed by myalgia (28%) and loss of smell or taste (28%); fever or rigors were reported in 21%. Neutralizing antibody titers in case patients during the peri-infection period were lower than those in matched uninfected controls (case-to-control ratio, 0.361; 95% confidence interval, 0.165 to 0.787).
- This multicenter, retrospective study conducted in USA among 189 patients aimed to examine the safety of the second dose of Pfizer-BioNTech or Moderna vaccine in those with a history of immediate and potentially allergic reactions to the first dose. Of the mRNA COVID-19 vaccine first-dose reactions evaluated, 130 (69%) were to Moderna and 59 (31%) to Pfizer-BioNTech. The most frequently reported first-dose reactions were flushing or erythema (53 [28%]), dizziness or lightheadedness (49 [26%]), tingling (46 [24%]), throat tightness (41 [22%]), hives (39 [21%]), and wheezing or shortness of breath (39 [21%]). Thirty-two (17%) met anaphylaxis criteria. A total of 159 patients (84%) received a second dose. Antihistamine premedication before the second dose was given in 47 patients (30%). All 159 patients, including 19 individuals with first-dose anaphylaxis, tolerated the second dose. Thirty-two (20%) reported immediate and potentially allergic symptoms that were associated with the second dose that were self-limited, mild, and/or resolved with antihistamines alone.
- This study analysed the development of anti-SARS-CoV-2 antibody and T cell responses in previously infected (recovered) or uninfected (naive) individuals that received mRNA vaccines. The authors found that previously infected individuals sustained higher antibody titers than uninfected individuals post-vaccination. The latter reached comparable levels of neutralization responses to the ancestral strain than previously infected individuals 7 days after the second vaccine dose. T cell activation markers measured upon spike or nucleocapsid peptide in vitro stimulation showed a progressive increase after

vaccination in the time-points analysed. Comprehensive analysis of plasma neutralization using 16 authentic isolates of distinct locally circulating SARS-CoV-2 variants revealed a range of reduction in the neutralization capacity associated with specific mutations in the spike gene: lineages with E484K and N501Y/T (e.g., B.1.351 and P.1) had the greatest reduction, followed by lineages with L452R (e.g., B.1.617.2) or with E484K (without N501Y/T). While both groups retained neutralization capacity against all variants, plasma from previously infected vaccinated individuals displayed overall better neutralization capacity when compared to plasma from uninfected individuals that also received two vaccine doses. [*not peer reviewed*]

- This cohort study aimed to determine the capacity of the BNT162b2 mRNA vaccine to induce effective cellular and humoral immune responses in people living with HIV/AIDS (PLWH). The study included 12 PLWH and 17 Healthy donors, none of the participants had evidence of prior SARS-CoV-2 infection. Blood samples were obtained between 7 and 17 days after the second vaccine dose. All PLWH were on antiretroviral therapy and had a median CD4+ T cell count of 913 cells/ul (range 649 to 1678 cells/ul). The authors report that there was no significant difference in titers of SARS-CoV-2 spike binding antibodies in healthy donors (median value of 9.49) and PLWH (median value of 8.84 p=0.07). Healthy donors and PLWH had similar levels of neutralizing antibodies to the vaccine strain spike protein and spike proteins from variants of concern (VOC) including the D614G, alpha (B.1.1.7), beta (B.1.351), and gamma (P.1) strains.
- This analysis of passive surveillance data aimed to assess the safety of the COVID-19 vaccination programme in Dalian, China. Data were collected from the Chinese National Adverse Events Following Immunization System (CNAEFIS). A total of 7.12 million doses of vaccine were administered from 27th November 2020 through 8th June 2021. There were 623 vaccinees who reported adverse events, resulting in a rate of 87.5 events per one million doses. The age-specific rates of AEFIs ranged from 74.0 per one million doses among persons aged 45 to 59 years to 102.0 per one million doses among persons aged 18 to 44 years; the manufacturer-specific rates ranged from 81.1 to 125.2 per one million doses. Among the 623 AEFIs, 544 (87.3%; rate, 76.4 per one million doses) were confirmed as common minor vaccine reactions. Very rare cases of anaphylaxis after vaccination were reported (5 cases; 0.7 per one million doses). Seven cases of AEFIs were classified as serious; however, available information indicated that there was no causal relationship with COVID-19 vaccination. [*not peer reviewed*]
- This study reports on the real-life effects of rapid mass vaccination campaign following a large outbreak of B.1.351 and B.1.1.7/E484K in the district of Schwaz, Austria. A total of 100,000 BNT162b2 doses were procured to mass vaccinate the entire adult population (16+) of the district between the 11th and 16th of March 2021. The authors compared the effect of the campaign on the number of infections including VOCs, hospital and intensive care unit (ICU) admissions in Schwaz with a control group of highly similar districts and with municipalities along the border of Schwaz which were excluded from the campaign. They found large and significant decreases for all outcomes after the campaign, including VOCs cases. The reduction relative to the control regions was largest for younger age cohorts, which were mostly non-vaccinated in the rest of the country due to the age-gradient in the national vaccination plan. Their results demonstrate that rapid population-wide mass vaccination can be an effective tool to curb overall infections as well as VOCs. [*not peer reviewed*]
- This study among health care workers in South Africa aimed to assess whether the time between infection and vaccination impacted the magnitude and breadth of boosted antibody and T cell responses, and to compare immunogenicity in the context of vaccine-matched and mismatched infection. The study included 60 HCWs who received Ad26.COV2.S vaccine (SARS-CoV-2 naive (n=20), infected during 1st wave before the emergence of Beta (n=20), and those infected in 2nd wave

(n=20), when Beta was the dominant variant). Their findings show that a priming exposure from infection significantly increased the magnitude of spike binding antibodies, neutralizing antibodies and antibody-dependent cellular cytotoxicity activity (ADCC) against D614G, Beta and Delta variants. The magnitude of antibody boosting was similar in both waves. ADCC and binding cross-reactivity was similar in both waves. [*not peer reviewed*]

- This matched test-negative case-control study aimed to estimate the effectiveness of an inactivated vaccine, CoronaVac, in healthcare workers (HCWs) in Manaus, Brazil where the Gamma variant was dominant. The authors performed an early analysis of effectiveness following administration of at least one vaccine dose (n=53,176) and an analysis of effectiveness of the two-dose schedule (n=53,153). 393 and 418 case-control pairs were selected for the early and two-dose analyses, respectively, matched on calendar time, age, and neighbourhood. In the early analysis, vaccination with at least one dose was associated with a 0.50-fold reduction (adjusted vaccine effectiveness (VE), 49.6%, 95% CI 11.3 to 71.4) in the odds of symptomatic SARS-CoV-2 infection during the period 14 days or more after receiving the first dose. However, they estimated low effectiveness (adjusted VE 36.8%, 95% CI -54.9 to 74.2) of the two-dose schedule against symptomatic SARS-CoV-2 infection during the period 14 days or more after receiving the second dose. Evidence from this test-negative study of the effectiveness of CoronaVac was mixed, and likely affected by bias. Their findings underscore the need to maintain non-pharmaceutical interventions while vaccination campaigns with CoronaVac are being implemented.

Diagnostics

- This study aimed to investigate dried blood spots (DBS) as an alternative sampling material for antibody detection by the automated Roche Elecsys Anti-SARS-CoV-2 anti-N immunoassay. The authors developed a semi-automated protocol using self-sampled DBS for SARS-CoV-2 serology. The protocol was validated in a cohort of matched DBS and venous-blood samples (n = 1710). Feasibility is demonstrated with two large serosurveys with 10247 company employees and a population cohort of 4465 participants. The authors report that sensitivity and specificity reached 99.20% and 98.65%, respectively. Providing written instructions and video tutorials, 99.87% (4465/4471) of the unsupervised home sampling DBS cards could be analysed. Their protocol might be useful for surveillance in resource-limited settings, providing low-cost highly accurate serology data.
- This prospective cross-sectional study aimed to assess the diagnostic test accuracy of two rapid antigen tests (Veritor System [Beckton Dickinson] and Biosensor [Roche Diagnostics]) in asymptomatic and presymptomatic close contacts of people with SARS-CoV-2 infection on day 5 after exposure. Of 2678 participants tested with Veritor, 233 (8.7%) had a RT-PCR confirmed SARS-CoV-2 infection of whom 149 were also detected by the rapid antigen test (sensitivity 63.9%, 95% CI; 57.4% to 70.1%). Of 1596 participants tested with Biosensor, 132 (8.3%) had a RT-PCR confirmed SARS-CoV-2 infection of whom 83 were detected by the rapid antigen test (sensitivity 62.9%, 54.0% to 71.1%). In those who were still asymptomatic, sensitivity was 58.7% (51.1% to 66.0%) for Veritor (n=2317) and 59.4% (49.2% to 69.1%) for Biosensor (n=1414), and in those who developed symptoms were 84.2% (68.7% to 94.0%; n=219) for Veritor and 73.3% (54.1% to 87.7%; n=158) for Biosensor. When a viral load cut-off was applied for infectiousness (≥5.2 log10 SARS-CoV-2 E gene copies/mL), the overall sensitivity was 90.1% (84.2% to 94.4%) for Veritor and 86.8% (78.1% to 93.0%) for Biosensor, and 88.1% (80.5% to 93.5%) for Veritor and 85.1% (74.3% to 92.6%) for Biosensor, among those who remained asymptomatic throughout. Specificities were >99%, and positive and negative predictive values were >90% and >95%, for both rapid antigen tests in all analyses.
- This study documents the large heterogeneity in longitudinal antibody responses (over 160 days) to SARS-CoV-2 across 14 commercial and research assays in a diverse cohort of 128 individuals. Measured responses in all binding assays correlated well with each other and, particularly for those measuring responses to spike protein, with pseudovirus neutralization. For all assays, the authors found a consistent, strong, and dose-dependent effect of disease severity on antibody magnitude.

Despite these similarities, assays performed quite differently in terms of sensitivity to detect prior infection and in the durability of measured responses, leading to large discrepancies in sensitivity between assays in the months following infection. Thus, the ability to detect previous infection by SARS-CoV-2 using an antibody test is highly dependent on the severity of the initial infection, when the sample is obtained relative to infection, and the assay used.

Care and Treatment

- This randomized, double-blind, placebo-controlled phase 3 trial aimed to evaluate the efficacy of canakinumab, an anti–interleukin-1β antibody, in patients hospitalized with severe COVID-19. The study included 454 hospitalized patients with severe COVID-19 not requiring invasive mechanical ventilation (IMV) and with elevated C-reactive protein or ferritin levels in 39 hospitals in Europe and the United States. Patients were randomly assigned 1:1 to receive a single intravenous infusion of canakinumab (n=227) or placebo (n=227). Treatment with intravenous canakinumab vs placebo resulted in survival without IMV at 29 days of 88.8% vs 85.7%, a difference that was not statistically significant.
- This cohort study among 13,001 adults in Norway aimed to examine self-reported memory problems 8 months after COVID-19 infection. The mean (SD) age was 47 (14.3) years, and 8642 (66%) were women. At follow-up, 9705 of 13 001 participants (75%) responded, and 72 of 651 of the participants (11%) in the SARS-CoV-2–positive group reported memory problems. In contrast, 254 of 5712 participants (4%) in the SARS-CoV-2–negative group or 80 of 3342 participants (2%) in the untested randomly selected reported memory problems. In the multiple logistic regression model, SARS-CoV-2 positivity at baseline was strongly associated with reporting memory problems at 8 months follow-up (odds ratio [OR], 4.66; 95% CI, 3.25-6.66) compared to the untested randomly selected group. At follow-up, in the SARS-CoV-2–positive group, 41% reported a significant worsening of health compared with 1 year prior, and 12% also reported problems concentrating.
- This review summarizes studies of the long-term effects of COVID-19 in hospitalized and non-hospitalized patients and describes the persistent symptoms they endure. The symptoms include fatigue, dyspnea, cardiac abnormalities, cognitive impairment, sleep disturbances, symptoms of post-traumatic stress disorder, muscle pain, concentration problems, and headache. The authors also discussed risk factors for acute COVID-19 and long COVID and possible therapeutic options.
- This meta analysis of 28 (26 cohort, 2 case-control) studies involving 12,995 COVID-19 patients aimed to analyze the potential association of dyslipidemia with the severity and mortality of COVID-19. The authors report that dyslipidemia was associated with the severity of COVID-19 (odds ratio [OR] = 1.27, 95% confidence interval [CI] 1.11-1.44, P = 0.038, I^2 = 39.8%). Patients with dyslipidemia had a 2.13-fold increased risk of death compared to patients without dyslipidemia (95% CI 1.84-2.47, P = 0.001, I^2 = 66.4%). They recommend monitoring of blood lipids and active treatment of dyslipidemia in COVID-19 patients to reduce severity and mortality.

Epidemiology

- This modelling study analysed the growth and dominance of the B.1.617.2 Delta variant in Mumbai. Their analysis implicates combined effects of immune evasion and increased transmissibility. The authors found significantly reduced sensitivity of B.1.617.2 to convalescent sera and sera from BNT162b and ChAdOx-1 vaccinees. They also found substantial loss of sensitivity to a large panel of spike specific monoclonal antibodies, including compromise of key monoclonals (imdevimab and bamlanivumab). B.1.617.2 appeared to confer an entry and replication advantage over B.1.617.1. In vaccinated health care workers, they found evidence for reduced ChAdOx-1 efficacy against B.1.617.2 relative to non-B.1.617.2. Their data indicate that (i) significant immune evasion and virus fitness are

both responsible for the observed global dominance of B.1.617.2, (ii) that health care settings should maintain infection control in settings where B.1.617.2 is prevalent and (iii) that REGN-COV2 combination therapy could be compromised by B.1.617.2, particularly in those with immune deficiency with concomitant risk of selection of escape mutants. [*not peer reviewed*]

- This report describes an outbreak of SARS-CoV-2 infections, including COVID-19 vaccine breakthrough infections, associated with large public gatherings in Barnstable County, Massachusetts that occurred in July 2021. A total of 469 COVID-19 cases were identified among Massachusetts residents who had traveled to the town for multiple summer events and large public gatherings during July 3–17; 346 (74%) occurred in fully vaccinated persons. Testing identified the Delta variant in 90% of specimens from 133 patients. Overall, 274 (79%) vaccinated patients with breakthrough infection were symptomatic. Among five COVID-19 patients who were hospitalized, four were fully vaccinated; no deaths were reported. Vaccine products received by persons experiencing breakthrough infections were Pfizer-BioNTech (159; 46%), Moderna (131; 38%), and Janssen (56; 16%); among fully vaccinated persons in the Massachusetts general population, 56% had received Pfizer-BioNTech, 38% had received Moderna, and 7% had received Janssen vaccine products. Cycle threshold values were similar among specimens from patients who were fully vaccinated and those who were not.
- This prospective cohort study in one rural and one urban community of South Africa from July 2020 to March 2021 aimed to estimate the burden and transmission of SARS-CoV-2 over the two waves. The authors collected mid-turbinate nasal swabs twice-weekly from consenting household members for rRT-PCR. Serum was collected every two months and tested for anti-SARS-CoV-2 antibodies. Among 71,759 nasal specimens from 1,189 members (follow-up rate 93%), 834 (1%) were SARS-CoV-2-positive. By PCR detection and serology combined, 34% (406/1189) of individuals experienced ≥1 SARS-CoV-2 infection episode, and 3% (12/406) experienced reinfection. 83% of SARS-CoV-2 infections were asymptomatic and index case symptom status did not affect Household cumulative infection risk (HCIR). Previous infection was protective against SARS-CoV-2 infection in the second wave although household transmission increased following the emergence of Beta variant. [*not peer reviewed*]
- This prospective cohort study among 96 patients in Germany, treated for acute COVID-19 between February and April 2020, tracked symptoms, quality of life, and antibody levels. Their findings show that 77.1% of patients reported 1 or more COVID-19 symptoms persisting up to 12 months post infection (56.3% reported reduced exercise capacity, 53.1% fatigue, 37.5% dyspnoea and 39.6% concentration problems, 32.3% problems finding words, and 26.0% sleeping problems). At 12 months post COVID-19 symptom onset, antinuclear antibody (ANA) titers were ≥1:160 in 43.6% of patients. This may indicate autoimmunity as cofactor in aetiology of long COVID.
- This systematic review and meta-analysis of 21 studies that involved more than 91 million individuals aimed to assess whether preexisting mood disorders are associated with a higher risk of COVID-19 susceptibility, hospitalization, severe complications, and death. The authors found a significantly higher odds of COVID-19 hospitalization (OR, 1.31; 95% CI, 1.12-1.53; $P = .001$; n = 26,554,397) and death (OR, 1.51; 95% CI, 1.34-1.69; $P < .001$; n = 25,808,660) in persons with preexisting mood disorders compared with those without mood disorders. There was no association between mood disorders and COVID-19 susceptibility (OR, 1.27; 95% CI, 0.73-2.19; n = 65,514,469) or severe events (OR, 0.94; 95% CI, 0.87-1.03; n = 83,240). Their results suggest that individuals with mood disorders should be categorized as an at-risk group for COVID-19 hospitalization and death, providing basis for vaccine prioritization.
- This retrospective cohort study aimed to determine the association between COVID-19 and preterm (PTB) birth among live births documented by California Vital Statistics birth certificates between July

2020 and January 2021 (n=240,157). The authors used best obstetric estimate of gestational age to classify births as very preterm (VPTB, <32 weeks), PTB (< 37 weeks), early term (37 and 38 weeks), and term (39-44 weeks). Their findings showed that COVID-19 diagnoses on birth certificates increased for all racial/ethnic groups during the study period. COVID-19 diagnosis was associated with an increased risk of VPTB (aRR 1.6, 95% CI [1.4, 1.9]), PTB (aRR 1.4, 95% CI [1.3, 1.4]), and early term birth (aRR 1.1, 95% CI [1.1, 1.2]). There was no effect modification of the overall association by race/ethnicity or insurance status. COVID-19 diagnosis was associated with elevated risk of PTB in people with hypertension, diabetes, and/or obesity.

- This observational study aimed to test whether there were consistent associations of symptoms with SARS-CoV-2 test status across three surveillance platforms in three countries (two platforms per country), during periods of testing and policy changes. The study population included adult respondents who were not healthcare workers in the UK, Israel, and the USA. Between April 1 and July 31, 2020, 514,459 tests from over 10 million respondents were recorded in the six surveillance platform datasets. Anosmia–ageusia was the strongest, most consistent symptom associated with a positive COVID-19 test (robust aggregated rank one, meta-analysed random effects OR 16.96, 95% CI 13.13–21.92). Fever (rank two, 6.45, 4.25–9.81), shortness of breath (rank three, 4.69, 3.14–7.01), and cough (rank four, 4.29, 3.13–5.88) were also highly associated with test positivity. The association of symptoms with test status varied by duration of illness, timing of the test, and broader test criteria, as well as over time, by country, and by platform.
- This modelling study developed a new method for estimating the epidemic growth rate and a framework for robust epidemic monitoring using information inherent in cycle threshold (Ct) values from reverse transcription quantitative polymerase chain reaction (RT-qPCR) tests. Their method performed well in estimating the epidemic trajectory in the state of Massachusetts using routine hospital admissions RT-qPCR testing data—accurately replicating estimates from other sources for the entire state.

Infection Prevention and Control

- This retrospective quality improvement study presents an innovation for COVID-19 outpatient testing in response to high testing demand and scarce availability of personal protective equipment (PPE). The authors designed a high-efficiency particulate air–filtered, positive-pressure personal protection booth with 6 ergonomic glove ports called a Hexapod. Hexapod use was associated with cost savings, decreased use of PPE, and increased testing throughput, suggesting that the use of the Hexapods helped address the aforementioned testing challenges.
- This study aimed to evaluate the ability of vapourised hydrogen peroxide (VHP) to inactivate SARS-CoV-2 bioburden on N95 Filtering Facepiece Respirators (FFRs) without compromising filtration efficiency. The authors also investigated coronavirus HCoV-229E as a surrogate for decontamination validation testing. The N95 FFRs were laced with SARS-CoV-2 or HCoV-229E and treated with VHP in a hospital reprocessing facility. The viral burden and filtration efficiency were then tested. The authors report that viable SARS-CoV-2 virus were not detected after VHP treatment. One replicate of the HCoV-229E laced FFRs yielded virus after processing. Unexpired N95 FFRs retained full filtration efficiency after VHP processing. Expired FFRs failed to meet design-specified filtration efficiency and therefore are unsuitable for reprocessing. HCoV-229E is found to be a suitable surrogate for SARS-CoV-2 for disinfection studies.

Non-pharmaceutical interventions, social distancing

- This cross-sectional study aimed to examine the extent to which mask mandates are followed and quantify the bias of self-reported mask usage in Siaya county, Kenya. The authors observed the

masking behaviour of 9533 individuals. They collected survey data from 1960 individuals who self-reported mask use at a total of 6225 public outings. They found a large and statistically significant discrepancy between self-reported and observed mask use. While only 12% of people admitted to not wearing a mask, 90% were observed not using them (77.7% difference; 95% CI, 80.9%-74.5%). The discrepancy between self-reports and observations persisted when they examined mask use by gender, age, and location. The proportion of correct mask use was significantly higher on public transportation than at markets or in villages.

- This study aimed to monitor the personal protective equipment (PPE) pollution associated with COVID-19 along the coastline of Agadir, Morocco. A total of 689 PPE items were identified, with a mean density of 1.13×10^{-5} PPE m^{-2} (0-1.21×10^{-4} PPE m^{-2}). The majority of the PPE items found were face masks (96.81%), out of which 98.4% were surgical masks and 1.6% were reusable cloth masks. The most polluted sites were the beaches with recreational activities, followed by surfing, and fishing as the main activity. Importantly, PPE density increased significantly after lockdown measures. They recommend significant efforts to raise environmental awareness, education on proper disposal of PPE, improving beach cleaning strategies and to penalise incorrect PPE disposal.
- This study summarizes various methods that can be used to enhance masks' protection performance and fabricate innovative masks with more advanced functions. These methods include i) boosting the antimicrobial and self-disinfectant characteristics via incorporating metal nanoparticles or photosensitizers, ii) increasing the self-cleaning by inserting superhydrophobic materials such as graphenes and alkyl silanes, iii) creating photo/electrothermal properties by forming graphene and metal thin films within the masks, and iv) incorporating triboelectric nanogenerators among the friction layers of masks to stabilize the electrostatic charges and facilitating the recharging of masks. The authors explain the effectiveness and limitations of each method in generating the desired properties.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 29th July 2021, Scancell Holdings plc announced that the South African Health Products Regulatory Authority (SAHPRA) has approved Phase 1 clinical study of its COVID 19 vaccine candidate, SCOV1 in South Africa. It is anticipated that the study will start in the second half of 2021. It will be conducted at the University of Cape Town Lung Institute, South Africa and will enroll unvaccinated, healthy adult volunteers. SCOV1 targets the original SARS-CoV-2 strain.
- On 23rd July 2021, Moderna, Inc. announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending marketing authorization for Moderna's COVID-19 vaccine (Spikevax) to include adolescents 12 years of age and older. This comes after data from the ongoing phase 2/3 study which enrolled 3,732 participants ages 12 to less than 18 years in the United States indicated a vaccine efficacy of 100%. Following the CHMP's positive opinion, the European Commission will consider authorizing use of the Moderna COVID-19 Vaccine in adolescents ages 12 years of age and older.
- On 19th July 2021, Shionogi & Company Limited and HanaVax Inc announced they have entered into a license agreement for development of novel nasal vaccine candidates for COVID-19 using HanaVax's cationic nanogel delivery system (cCHP). As per the agreement, Shionogi is granted exclusive global rights to research, develop, manufacture, distribute, and commercialize COVID-19 nasal vaccines using cCHP technology while HanaVax will receive an upfront payment and milestones relating to future development progress, as well as royalties based on net sales of the vaccine. cCHP is a unique delivery technology using cationic cholesteryl group-bearing pullulan which when administered intranasally, can effectively induce immunity in the respiratory mucosa, and the whole body.

Therapeutics trials:

- On 27th July 2021, BetterLife Pharma Inc. announced that its subsidiary, Altum Pharmaceuticals Inc. and Pontificia Universidad Católica de Chile have obtained approval from the Instituto de Salud Publica de Chile to conduct a randomized placebo-controlled trial for its inhaled drug candidate, AP-003, for treating Covid-19 patients in Chile. The trial will start in early August and intends to enroll healthy subjects in phase I and early stage COVID 19 patients in phase II.
- On 27th July 2021, NRx Pharmaceuticals announced that the Nation of Georgia's Prime Minister and Minister of Health have issued an Emergency Use Authorization for intravenous ZYESAMI™ (aviptadil) for the treatment of Critical COVID-19 patients. This comes when the nation is observing increases in COVID-19 cases, hospitalized patients, and patients in hospital intensive care units. The decision has been unanimously supported by the Association of Georgian Physicians.
- On 26th July 2021, Trevena, Inc. announced the first COVID-19 patient has been enrolled in the ACTIV-4 (Accelerating COVID-19 Therapeutic Interventions and Vaccines) Host Tissue trial which is analyzing its drug, TRV027, for the treatment of Covid-19. TRV027 is a novel AT_1 receptor selective agonist that specifically binds to and rebalances AT_1 receptor activation within the renin-angiotensin-aldosterone system (RAAS). The multi-centre, randomized, placebo-controlled ACTIV-4 Host Tissue trial will analyze four investigational agents that address Covid-19-induced dysregulation of the RAAS and the immune system. The trial will enroll approximately 1,600 patients at over 50 sites in the U.S. The trial is funded by National Institutes of Health (NIH).
- On 26th July 2021, Shionogi and Company Limited announced that it has initiated a Phase 1 clinical trial of its therapeutic agent S-217622, an oral antiviral drug for the treatment of COVID-19 in Japan. The first dose in the trial was given on 22 July 2021 and no safety concerns have been reported. S-217622 suppresses the duplication of SARS-CoV-2 by selectively inhibiting 3CL protease, an enzyme produced by SARS-CoV-2 virus which is essential for its duplication.
- On 22nd July 2021, Innovation Pharmaceuticals announced the results of an in vitro study of its drug candidate, brilacidin, that demonstrated its broad-spectrum antiviral potential to SARS-CoV-2. Data shows that brilacidin, a host defense protein/peptide mimetic, has potential ability to hinder the SARS-CoV-2 virus in various human cell lines, including Caco-2, which is primary lung fibroblasts, alphaviruses such as Venezuelan equine encephalitis virus, Eastern equine encephalitis virus and Rift Valley fever virus, a bunyavirus. These data are based on the study carried out by researchers at the George Mason University (GMU)/National Center for Biodefense and Infectious Diseases in the US.
- On 20th July 2021, Regeneron Pharmaceuticals, Inc. announced that Japan's Ministry of Health, Labour and Welfare (MHLW) has approved Regeneron's casirivimab and imdevimab antibody cocktail to treat patients with mild to moderate COVID-19. The approval was based on results from a Phase 3 trial in high-risk non-hospitalized patients, which showed the antibody cocktail reduced the risk of hospitalization or death by 70%, as well as results from a Phase 1 trial that examined the safety, tolerability and pharmacokinetics in Japanese people. Japan becomes the first country to fully approve regeneron antibody cocktail (casirivimab and imdevimab) for the treatment of mild to moderate covid-19.
- On 19th July 2021, NRx Pharmaceuticals reported findings of its completed randomized phase 2b/3 trial that indicated a statistically significant effect of ZYESAMI™ (aviptadil) in preventing sharp rise in cytokines, commonly associated with mortality in patients with COVID-19. As per the data, patients treated with placebo experienced a statistically significant elevation in interleukin 6 (IL-6) cytokine levels, whereas those treated with ZYESAMI™ had a minimal increase in IL-6. The anti-cytokine effect of ZYESAMI™ was additionally associated with a significant decrease in 60-day mortality. NRx has submitted biomarker letter of intent based on these findings to US Food and Drug Administration (FDA) as a supplement to its pending application for Emergency Use Authorization for ZYESAMI™.
- On 15th July 2021, Kintor Pharmaceutical Limited announced that it has entered into a licensing agreement with Shanghai Fosun Pharmaceutical Development Limited on the commercialization of proxalutamide, an androgen receptor (AR) antagonist, for the treatment of COVID-19 in India and 28 African countries. Kintor and Fosun Pharma Development will both work on the emergency use authorization applications, promotion, and sales of proxalutamide. At the moment, there are two

registered phase III multi-regional clinical trials (MRCT) of proxalutamide for the treatment of COVID-19 outpatients, and one phase III MRCT for COVID-19 inpatients being conducted in countries and regions including the United States, South America (including Brazil), the European Union, and Asia.

For further detailed information for each country, refer to the full table here

E. Public Health and Social Measures

The table highlights changes in public health and social measures (PHSMs) based on data from the Oxford COVID-19 Government Response Tracker. An up arrow indicates new PHSMs were announced; a horizontal arrow indicates PHSM were extended; a down arrow indicates PHSMs were loosened/expired. Member States are organized by tiers based on current epidemiological data from 24th to 30th July 2021.

Country	PHSM Trend	PHSM Change
Tier 4 (High Alert): Daily case incidence per 1M people/day ≥ 80 and/or positivity rate ≥ 12%		
Libya	↑	Officials in **Libya** imposed a nationwide nightly curfew, from 18:00-06:00, currently enforced by the military.
Morocco	→/↑	**Morocco** extended the nationwide state of health emergency until 10 September. The city of Casablanca was also put into lockdown, which includes a nightly curfew and school closures.
Rwanda	→	Authorities in **Rwanda** extended lockdown measures in capital city Kigali and surrounding districts through 31 July. Measures include a stay-at-home order for nonessential travel, a ban on public gatherings, and capacity limits on public transport and in other businesses.
South Africa	↑	Some restrictions to prevent the spread of COVID-19 have been lifted in **South Africa**, including the ban on the sale of alcohol and restrictions on movement between provinces. Other measures--including the mask mandate--remain in place.
Tunisia	↑	The president of **Tunisia** imposed a strict nightly curfew, a ban on public gatherings of 3 or more, and dismissed parliament, a move many are calling a coup in response to intense protests against the government handling of COVID.
Zimbabwe	↓	Although other nationwide lockdown measures remain in place, **Zimbabwe** is reopening some of its tourist attractions to vaccinated visitors, including the famous Victoria Falls.
Tier 3 (Moderate Alert): Daily case incidence per 1M people/day is 20 to <80 and/or positivity rate is 5% to <12%		
Algeria	↑	The nightly curfew in **Algeria** was extended by 5 hours (from 20:00-6:00, previously 23:00-4:00) and imposed additional restrictions, including closure of gyms and beaches, and takeout service only at restaurants and cafes.

Cabo Verde	↓	Authorities in **Cabo Verde** allowed the nationwide state of calamity to lapse given the current epidemiological situation in the country. Restrictions on activities and gatherings will be lifted for people who can show proof of vaccination.
Lesotho	↑	**Lesotho** increased their nationwide alert level from blue to purple. Measures under this order include a nightly curfew, capacity limits on religious services, and a ban on public and private social gatherings.
Mauritania	↑	Authorities in **Mauritania** extended the nationwide nightly curfew by two hours, from 22:00-6:00 to 20:00-6:00.
Tier 2 (Low Alert): Daily case incidence per 1M people/day is 5 to <20 and/or positivity rate is 3% to 5%		
Ghana	↑	Officials in **Ghana** imposed some restrictions on certain public gatherings, including time limits on funerals and a ban on post-wedding receptions.
Guinea-Bissau	→	**Guinea-Bissau** extended the nationwide state of alert until 8 August. Measures include capacity restrictions on social and cultural events (including funerals), ongoing closure of gyms and nightclubs, and a public mask mandate.
Tier 1 (Standard Precautions): Daily case incidence per 1M people/day is <5 and/or positivity rate is <3%		
Congo	↑/→	**Congo** banned flights from neighboring Democratic Republic of Congo due to concerns over the circulation of the Delta variant. Authorities in **Congo** also extended the nationwide state of health emergency until 13 August.
Madagascar	→	**Madagascar** extended the nationwide state of health emergency for an additional 15 days. Measures include nightly curfews in specific regions of higher transmission, as well as a mandate requiring the use of facemasks in public.

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