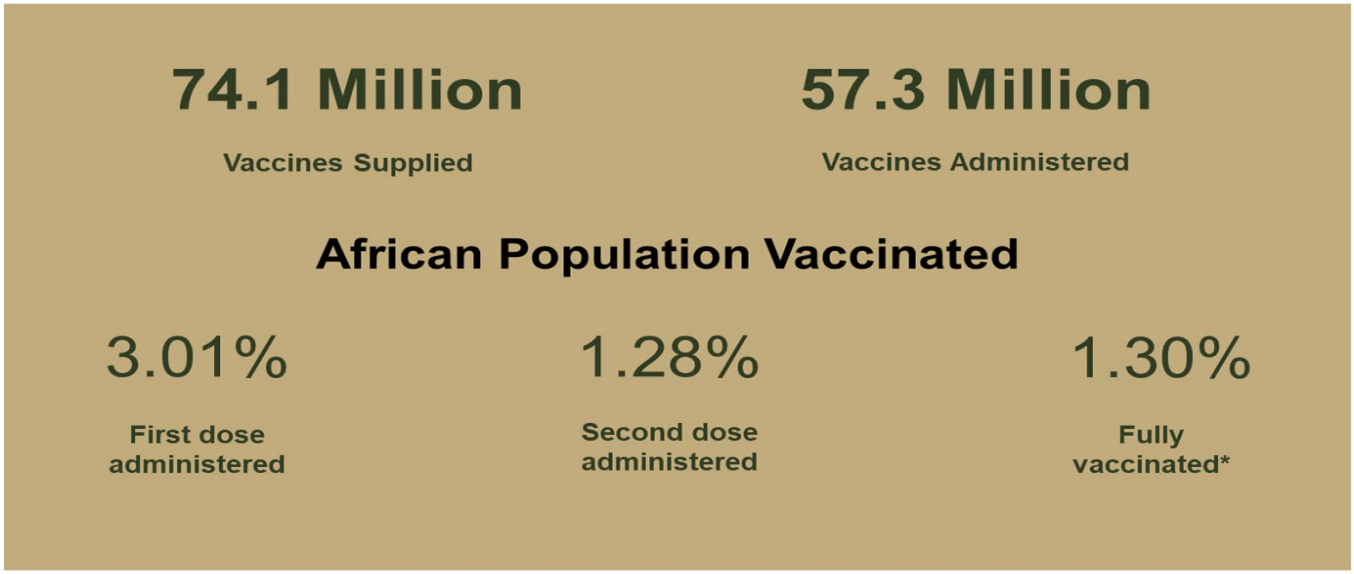
COVID-19 Scientific and Public Health Policy Update[1] – (20 July 2021)

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

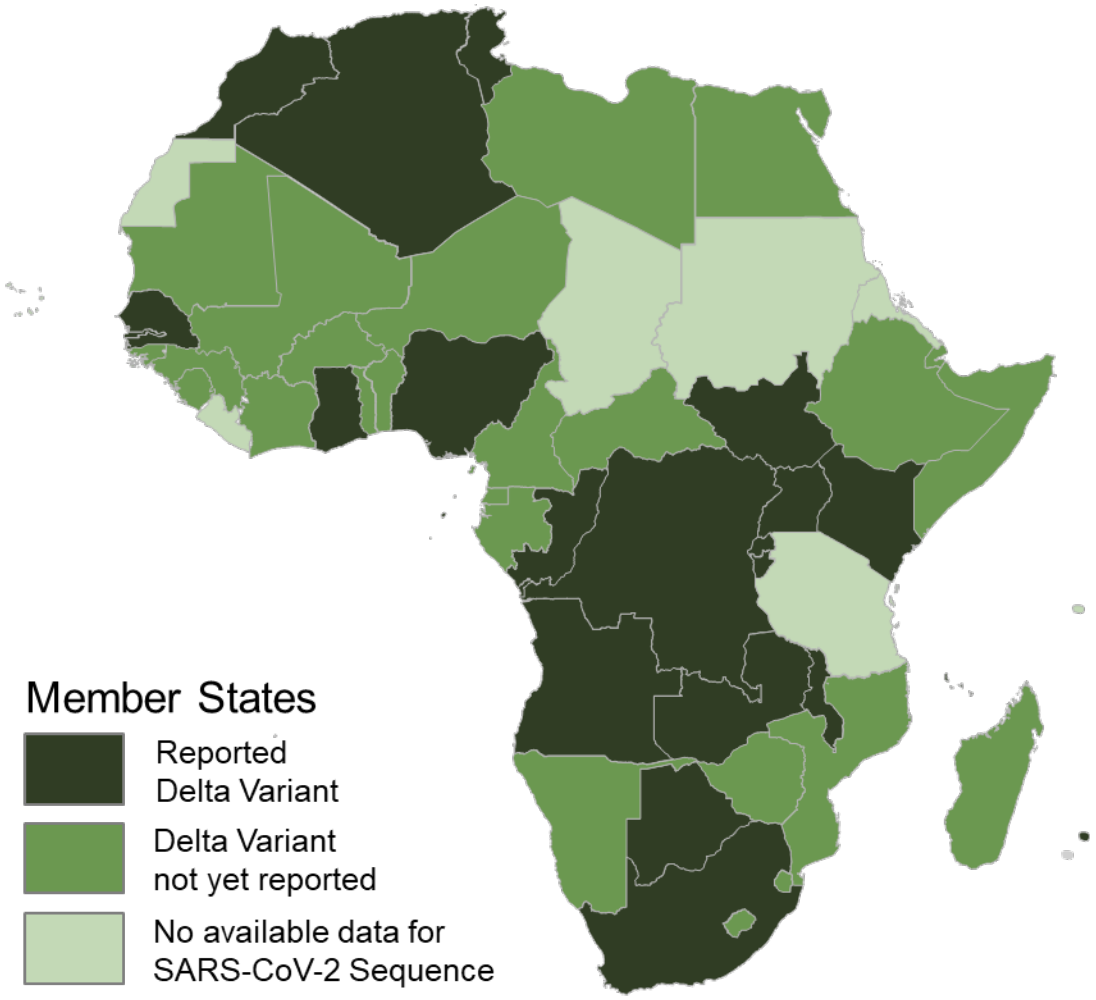


*Received two doses/ one dose of Johnson & Johnson vaccine
https://africacdc.org/covid-19-vaccination/
Updated 14th July 2021

Variants of Concern

- The B.1.617.2 (Delta variant), first reported in India, has spread to more than 111 countries worldwide; 20 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 14th July 2021

B. New guidelines and resources

Since 3rd July 2021,

- Africa CDC has published new guidance and resources on:
  - FAQs: Saving lives and livelihoods: the Africa CDC programme to support member states to rollout covid-19 vaccinations supported by mastercard foundation
  - Biosafety and Biosecurity Initiative 2021 – 2025 Strategic Plan
- US CDC has published new guidance and resources on:
  - Interim Public Health Recommendations for Fully Vaccinated People
  - Guidance for General Laboratory Safety Practices during the COVID-19 Pandemic
  - Guidance for Adult Day Services Centers
  - Key Operational Considerations for Jurisdictions Planning to Operate COVID-19 Vaccination Clinics
  - Expanding COVID-19 Vaccine Distribution to Primary Care Providers to Address Disparities in Immunization
  - COVID-vaccine-breakthrough-case-investigations-Protocol
  - COVID-19 Guidance for Operating Early Care and Education/Child Care Programs
  - Guidance for COVID-19 Prevention in K-12 Schools
  - Interim Guidance on People Experiencing Unsheltered Homelessness
- WHO has published new guidance and resources on:

- Clinical features and prognostic factors of COVID-19 in people living with HIV hospitalized with suspected or confirmed SARS-CoV-2 infection
- WHO technical consultation on oxygen access scale-up for COVID-19
- Safe Eid al Adha practices in the context of COVID-19
- Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed
- COVID-19 Vaccines: safety surveillance manual. Module on safety surveillance of COVID-19 vaccines in pregnant and breastfeeding women
- Diagnostics, therapeutics, vaccine readiness, and other health products for COVID-19
- Modelling the health impacts of disruptions to essential health services during COVID-19
- WHO Global Clinical Platform for the Clinical Characterization of COVID-19: Statistical Analysis Plan
- Therapeutics and COVID-19: living guideline
- Considerations for strengthening legal frameworks for digital contact tracing and quarantine tools for COVID-19

- FDA has issued press releases on:
  - FDA issued an Emergency Use Authorization (EUA) to Ortho-Clinical Diagnostics, Inc., for the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Test
  - Joint CDC and FDA Statement on Vaccine Boosters
  - As of 16th July, 396 tests and sample collection devices are authorized by the FDA under emergency use authorizations (EUAs).

- ECDC has issued new resources on:
  - COVID-19 in children and the role of school settings in transmission - second update

- PHE has issued new guidance and press releases on:
  - Guidance for supported living services during coronavirus (COVID-19)
  - Coronavirus (COVID-19): admission and care of people in care homes

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 examined the utility of serum neurofilament light chain (NFL), a neuroaxonal injury marker, in determining the frequency, severity and clinical consequences of neuronal damage in a cohort of 142 hospitalized patients with COVID-19. The authors measured NFL in 488 serum samples using the NF-Light digital immunoassay from Quanterix. They report that NFL was elevated in the serum of patients with COVID-19 compared to healthy controls, including those without overt neurological manifestations. Higher NFL serum concentrations were associated with worse clinical outcomes. In 100 hospitalized patients with COVID-19 treated with remdesivir, a trend toward lower NFL serum concentrations was observed. These data suggest that patients with COVID-19 may experience neuroaxonal injury and may be at risk for long-term neurological sequelae.
- This study examined the functional and structural consequences of SARS-CoV-2 infection in a reconstructed human bronchial epithelium (MucilAir™) model. The authors found that SARS-CoV-2 replication lead to a rapid loss of the ciliary layer, characterized at the ultrastructural level by axoneme loss and misorientation of remaining basal bodies. The extensive cilia loss was preceeded by a downregulation of the master regulator of ciliogenesis Foxj1, implicating this transcription factor in the

dedifferentiation of ciliated cells. Motile cilia function was compromised by SARS-CoV-2 infection, as measured in a mucociliary clearance assay. Analysis of SARS-CoV-2 infection in Syrian hamsters further demonstrated the loss of motile cilia in vivo. This study identified cilia damage as a pathogenic mechanism that could facilitate SARS-CoV-2 spread to the deeper lung parenchyma.

- This study used a mouse model to characterize SARS-CoV-2 entry cells in multiple sensory systems. The authors mapped the gene and protein expression of ACE2/TMPRSS2 in the mouse olfactory and gustatory cells, they precisely identified the virus target cells to be of basal and sensory origin (chemosensing). They found that the expression of viral entry sites in sensory cells increased with age, which might be an important factor for viral infectivity studies. They suggest a direct correlation between human sensory-symptomatology and mice SARS-CoV-2-expressing entry cells providing a putative explanation for the observed anosmia and ageusia in COVID-19 patients.
- This study in ferrets aimed to investigate the impact of male sex and age on SARS-CoV-2 infection. The authors compared sex-matched or age-matched ferrets infected with SARS-CoV-2. They identified differences in temperature regulation in male ferrets which was accompanied by prolonged viral replication in the upper respiratory tract after infection. Gene expression analysis of the nasal turbinates indicated that 1-year-old female ferrets had significant increases in interferon response genes post infection which were delayed in males. Their results provide insight into COVID-19 and suggest that older males may play a role in viral transmission due to decreased antiviral responses.
- This study reports on the in vitro effects of long chain, inorganic polyphospates (polyPs) of various lengths on SARS-CoV-2. Molecular docking and binding analyses showed that polyPs bound to the host receptor ACE2, which facilitates viral entry, and in viral RNA-dependent RNA polymerase (RdRP) required for replication. Both proteins underwent proteasomal degradation in cells incubated with polyP120, the optimal species tested, resulting in inhibition of SARS-CoV-2 replication and a reduced inflammatory response. They recommend further exploration of the potential therapeutic use of polyPs.
- This study in old mice infected with a SARS-CoV-2 related virus showed that treatment with senolytics reduced mortality and increased antiviral antibodies. Cellular senescence is a state elicited in response to stress signals and is associated with a damaging secretory phenotype. The number of senescent cells increases with advanced age and this in turn drives age-related diseases. Their findings strongly support the Geroscience hypothesis that therapeutically targeting fundamental aging mechanisms improves resilience in the elderly, with alleviation of morbidity and mortality due to pathogenic stress. This suggests that senolytics might protect others vulnerable to adverse COVID-19 outcomes in whom increased senescent cells occur (such as in obesity or numerous chronic diseases).

Vaccines

- This double-blind, randomised, placebo-controlled, case-driven phase 3 trial aimed to assess the safety and efficacy of the inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac) among volunteers aged 18-59 years across 24 centers in Turkey. The study included 11,303 volunteers. The authors report that CoronaVac had high efficacy for preventing symptomatic COVID-19 (83.5% relative to placebo) and COVID-19-related hospitalisation (100%) at least 14 days after the second dose. The most common systemic adverse event was fatigue (546 [8.2%] participants in the vaccine group and 248 [7.0%] in the placebo group, p=0.0228). Injection-site pain was the most frequent local adverse event (157 [2.4%] in the vaccine group and 40 [1.1%] in the placebo group, p<0.0001).
- This test-negative design study aimed to estimate the effectiveness of BNT162b2, mRNA-1273, and ChAdOx1 vaccines against symptomatic SARS-CoV-2 infection and severe outcomes (COVID-19 hospitalization or death) caused by the Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (B.1.617.2) variants of concern (VOCs) during December 2020 to May 2021. The authors used linked population-wide vaccination, laboratory testing, and health administrative databases in Ontario, Canada. Their findings suggest that even a single dose of these 3 vaccine products provide good to excellent protection against symptomatic infection and severe outcomes caused by the 4 currently circulating variants of concern, and that 2 doses are likely to provide even higher protection. [*not peer reviewed*]
- This prospective national cohort study in Chile aimed to assess the effectiveness of the inactivated SARS-CoV-2 vaccine (CoronaVac) with regard to preventing COVID-19 and related hospitalization,

admission to the ICU, and death. The study included approximately 10.2 million people who were 16 years of age or older. The authors found that among persons who were fully immunized, the adjusted vaccine effectiveness was 65.9% (95% CI, 65.2 to 66.6) for the prevention of COVID-19 and 87.5% (95% CI, 86.7 to 88.2) for the prevention of hospitalization, 90.3% (95% CI, 89.1 to 91.4) for the prevention of ICU admission, and 86.3% (95% CI, 84.5 to 87.9) for the prevention of COVID-19–related death. The findings are consistent with results of phase 2 trials of the vaccine.

- This study reports on the reduced sensitivity of SARS-CoV-2 variant Delta (B.1.617.2) to antibody neutralization. The authors isolated an infectious Delta strain from a traveller returning from India. They examined its sensitivity to monoclonal antibodies (mAbs) and to antibodies present in sera from COVID-19 convalescent individuals or vaccine recipients, in comparison to other viral strains. Variant Delta was found to be resistant to neutralization by some anti-NTD and anti-RBD mAbs including Bamlanivimab, which were impaired in binding to the Spike. Sera from convalescent patients collected up to 12 months post symptoms were 4 fold less potent against variant Delta, relative to variant Alpha (B.1.1.7). Sera from individuals having received one dose of Pfizer or AstraZeneca vaccines barely inhibited variant Delta. Administration of two doses generated a neutralizing response in 95% of individuals, with titers 3 to 5 fold lower against Delta than Alpha
- This study used the Hannover Medical School's COVID-19 Contact (CoCo) Study cohort of healthcare professionals to monitor ChAdOx1-nCov-19 (ChAd)-primed immune responses before and 3 weeks after booster with ChAd ($n = 32$) or BioNTech/Pfizer's BNT162b2 ($n = 55$). The authors report that although both vaccines boosted prime-induced immunity, BNT162b2 induced significantly higher frequencies of spike-specific CD4+ and CD8+ T cells and, in particular, high titers of neutralizing antibodies against the B.1.1.7, B.1.351 and P.1 variants of concern of SARS-CoV-2.
- This study describes the 8-month durability of humoral and cellular immune responses in 20 participants who received the Ad26.COV2.S vaccine in one or two doses (either 5×10^{10} viral particles or 10^{11} viral particles) and in 5 participants who received placebo. The authors evaluated antibody and T-cell responses on day 239, which was 8 months after the single-shot vaccine regimen (in 10 participants) or 6 months after the two-shot vaccine regimen (in 10 participants). Antibody responses were detected in all vaccine recipients on day 239. The median CD8+ T-cell response was 0.0545% on day 57, 0.0554% on day 85, and 0.0734% on day 239; the median CD4+ T-cell responses were 0.0435%, 0.0322%, and 0.0176%, respectively. The authors also report neutralizing antibody responses against the parental WA1/2020 strain of SARS-CoV-2, as well as against the SARS-CoV-2 variants D614G, B.1.1.7 (alpha), B.1.617.1 (kappa), B.1.617.2 (delta), P.1 (gamma), B.1.429 (epsilon), and B.1.351 (beta). Their results further support the use of the Ad26.COV2.S vaccine to combat the global COVID-19 pandemic.
- This study analysed immune responses following vaccination with the BNT162b2 mRNA vaccine in elderly participants and younger healthcare workers (n = 140, median age 72 years). The authors then followed them up to 3 weeks after 2nd dose (n=39). Antibody levels, serum neutralization and T-cell function were compared for persons <80 and ≥80 years of age after 1st and 2nd doses. Their results show that SARS-CoV-2 virus neutralization after 1 dose of BNT162b2 drops off precipitously at age 80 years. Following 2 doses, persons <80 years (n = 15) and ≥80 years (n = 24) show detectable neutralizing titers against B.1.1.7 (Alpha), B.1.351 (Beta) and P.1 (Gamma) variants of concern. Serum neutralization against wild-type, B.1.1.7, and B.1.351 was lower among persons ≥ 80 years compared to <80 years.
- This study compared vaccine-elicited antibody responses of patients with autoimmune diseases (n = 480) to healthy controls (n = 204) from two ongoing prospective cohort studies. Post-vaccination sera were analyzed by receptor binding domain (RBD) antibody ELISAs and compared by treatment type. The authors report that after 1st dose of BNT162b2, ChAdOx1, or CX021414 (Moderna) COVID-19 vaccines, neutralizing antibody (NAb) anti-receptor binding domain IgG levels were lower for COVID-19 naïve patients on methotrexate or anti-CD20 compared to healthy controls. Compared to 71% of healthy controls, 25% of 111 patients on methotrexate and none of 15 patients on anti-CD20 therapies seroconverted. After 2nd vaccine dose, except for those on anti-CD20 therapies, more than 88% of all patient groups seroconverted. Their results suggest that two doses of COVID-19 vaccines effectively

generate an immune response among patients who are being treated with many immunomodulatory therapies, except anti-CD20 monoclonal antibodies. [*not peer reviewed*]

- This prospective UK serological study reports on vaccine-induced neutralizaing antibody activity in recipients of AZD1222 (Oxford/AstraZeneca) (n = 63) compared with BNT162b2 (Pfizer/BioNTech) (n = 159). The authors measured median virus neutralizing antibody (Nab) titers against 5 variants [Wild-type, D614G, B.1.1.7 (Alpha), B.1.351 (Beta), B.1.617.2 (Delta)], after 1 and 2 vaccine doses. Virus NAb response elicited against the 5 variants after 2 doses of AZD1222 were at least 2-fold lower relative to 2 doses of BNT162b2. Neutralizing antibodies were reduced 2.5-fold against B.1.351 and B.1.617.2. Their results suggest that AZD1222 offers less protection against SARS-CoV-2 variants, including the B.1.617.2 Delta variant.
- This study aimed to describe a group of patients with acute myocarditis over a 3 months period between February 1 and April 30, 2021 who were referred for cardiovascular magnetic resonance imaging at Duke University Medical Center. The authors identified 7 patients with acute myocarditis, of which 4 occurred within 5 days of COVID-19 vaccination. Three were younger male individuals (age, 23-36 years) and 1 was a 70-year-old female individual. All 4 had received the second dose of an mRNA vaccine (2 received mRNA-1273 [Moderna], and 2 received BNT162b2 [Pfizer]). All presented with severe chest pain, had biomarker evidence of myocardial injury, and were hospitalized. Coincident testing for COVID-19 and respiratory viruses provided no alternative explanation. Cardiac magnetic resonance imaging findings were typical for myocarditis, including regional dysfunction, late gadolinium enhancement, and elevated native T1 and T2.
- This study used sera collected 71 days post vaccination with Ad26.COV2.S (Johnson & Johnson/Janssen) from 8 participants in a phase 3 clinical trial (age range: 47–91) and tested for neutralizing activity against SARS-CoV-2 variants of concern including B.1.351 (Beta), P.1 (Gamma), and B.1.617.2 (Delta). The authors report that compared to B.1, a single dose of Ad26.COV2.S vaccine had reduced neutralization sensitivity to SARS-CoV-2 variants B.1.351 (3.6-fold less), P.1 (3.4-fold less), and B.1.617.2 (1.6-fold less). [*not peer reviewed*]
- This study used sera post vaccination with BNT162b2 or ChAdOx1 from 155 healthy individuals (≥18 years old) in the UK COVID-19 Deployed Vaccine Cohort Study (DOVE). The authors tested for neutralizing antibody production against SARS-CoV-2 spike protein-pseudotyped HIV for the B.1.617.1 and B.1.617.2 and B.1.351 variants. Their findings show that antibody titers produced by 2 doses of BNT162b2 (Pfizer/BioNTech) neutralized B.1.617.2, B.1.617.1, and B.1.351 variants 7.8-, 11.3-, and 9.6-fold less effectively than wild-type SARS-CoV-2. Differences in neutralization against variants produced by ChAdOx1 were not significant. Mean antibody titers against all Wuhan strains were significantly higher in individuals vaccinated with BNT162b2 than in those vaccinated with ChAdOx1. Their results indicate that BNT162b2 and ChAdOx1 vaccines induced neutralizing antibodies may be less efficient at targeting the B.1.617.2 variant compared to wild-type SARS-CoV-2. [*not peer reviewed*]
- This study among volunteers aged 18-55 years who were enrolled in a phase 1/2 or phase 2/3 clinical trial of ChAdOx1 nCoV-19 (AZD1222) and had received either a single dose or two doses of the vaccine assessed the persistence of immunogenicity after a single dose, the immunity after an extended interval between the first and second dose of the vaccine, and the response to a third dose as a late booster. The authors report that the median antibody titers after dose 2 of ChAdOx1 increased from 923 EU at 8–12 weeks to 3738 EU at 44–46 weeks. Among a subset of 75 participants, antibody titers further increased after a third dose compared with 28 days after dose 2, including against Alpha (B.1.1.7), Beta (B.1.351) and Delta (B.1.617.2) variants in 45 participants. T-cell responses were also boosted after a 3rd dose. Their results show that a longer delay before the second dose of ChAdOx1 nCoV-19 leads to an increased antibody titre after the second dose. A third dose of ChAdOx1 nCoV-19 induces antibodies to a level that correlate with high efficacy after second dose and boosts T-cell responses. [*not peer reviewed*]
- This single-center, open-label, non-randomized, Phase 1/2 trial in India aimed to assess the safety and immunogenecity of a DNA SARS-CoV-2 vaccine candidate (ZyCov-D). The vaccine comprises a DNA plasmid Vector pVAX1 carrying gene expressing spike-S protein of SARS-CoV-2 and IgE signal peptide. The authors enrolled 48 participants in the study. Their results show that 12/48 (25%) subjects reported at least one adverse event during the study. There were no deaths or serious adverse events

reported. The proportion of subjects who seroconverted based on IgG titers on day 84 was 4/11 (36.36%), 4/12 (33.33%), 10/10 (100.00%) and 8/10 (80.00%) in the treatment Arm 1 (1 mg: Needle), Arm 2 (1 mg: Needle-Free injection System[NFIS]), Arm 3 (2 mg: Needle) and Arm 4 (2 mg: NFIS), respectively.

- This double-blind, randomised, controlled, phase 1/2 clinical trial of CoronaVac aimed to assess the safety, tolerability, and immunogenicity of a candidate COVID-19 vaccine, CoronaVac, in children and adolescents aged 3–17 years in Hebei, China. The study enrolled 552 participants (72 in the phase I and 480 in the phase II clinical study). The results indicated that CoronaVac was well tolerated and safe and induced humoral responses in children and adolescents aged 3–17 years. Neutralising antibody titres induced by the 3·0 µg dose were higher than those of the 1·5 µg dose. The results support the use of 3·0 µg dose with a two-immunisation schedule for further studies in children and adolescents.
- This phase 3, randomized, observer-blinded, placebo-controlled trial conducted at 33 sites in the United Kingdom reports on the efficacy, immunogenicity, and safety of NVX-CoV2373 vaccine (Novavax) in a larger population. A total of 14,039 were included in the per-protocol efficacy population. Adults between the ages of 18 and 84 years were included and doses of NVX-CoV2373 or placebo were administered 21 days apart. The results demonstrated that a two-dose regimen of the NVX-CoV2373 vaccine administered to adult participants conferred 89.7% protection against SARS-CoV-2 infection and showed high efficacy against the B.1.1.7 variant.

Diagnostics

- This pilot study among 163 healthy adults (aged ≥ 18 years) from a single college campus COVID-19 screening site aimed to evaluate the feasibility of a novel, objective olfactory test as part of an initial screening for COVID-19 in adults with unknown disease status. The participants were screened for olfactory dysfunction (OD) using a novel scent card (SAFER Diagnostics) followed by SARS-CoV-2 PCR testing. Of those who tested PCR-positive for COVID-19, 75% (12 out of 16) failed olfactory screening compared with 4.8% (7 out of 147) among those testing PCR-negative for COVID-19. The sensitivity, specificity, positive predictive value, and negative predictive value of the scent card in detecting those with COVID-19 were 75.0%, 95.2%, 63.2%, and 97.2%, respectively. Including the symptom fatigue along with OD achieved a 93.8% sensitivity and 89.8% specificity in disease screening.
- This study aimed to assess the diagnostic accuracy of antigen detection via lateral flow testing (LFT) compared to RT-PCR on the same primary-care patients in Austria. The study included 2562 symptomatic patients (with mild/moderate flue-like symptoms). A total of 1,037 patients were suspected of COVID-19 and 826 (79.7%) patients tested RT-PCR positive. Among patients with positive RT-PCR, 788/826 tested LFT reactive and 38 (4.6%) non-reactive. Overall sensitivity was 95.4% (95%CI: [94%,96.8%]), specificity 89.1% (95%CI: [86.3%, 91.9%]), positive predictive value 97.3% (95%CI:[95.9%, 98.7%]) and negative predictive value 82.5% (95%CI:[79.8%, 85.2%]). Reactive LFT and positive RT-PCR were positively correlated (r = 0.968, 95CI=[0.952,0.985] and κ=0.823, 95%CI=[0.773,0.866]).
- This observational cohort study aimed to assess the performance of the Innova SARS-CoV-2 antigen rapid lateral flow test (LFT) versus RT-qPCR testing in the asymptomatic general population attending 48 testing centres in Liverpool, UK. The study involved 5869 asymptomatic adults (≥18 years). The authors report that of 5869 test results, 22 (0.4%) LFT results and 343 (5.8%) RT-qPCR results were void. Excluding the void results, the LFT versus RT-qPCR showed a sensitivity of 40.0% (95% CI; 28.5% to 52.4%), specificity of 99.9% (95%CI: 99.8% to 99.99%), positive predictive value of 90.3% (95%CI: 74.2% to 98.0%), and negative predictive value of 99.2% (95%CI: 99.0% to 99.4%).

Care and Treatment

- This retrospective cohort study aimed to examine associations between remdesivir treatment and survival and length of hospital stay among people hospitalized with COVID-19 in routine care settings. The authors used data from the Veterans Health Administration (VHA) to identify 5898 adult patients in 123 VHA hospitals who had a first hospitalization with laboratory-confirmed COVID-19 from May 1 to October 8, 2020. After propensity score matching, the analysis included 1172 remdesivir recipients and 1172 controls, for a final matched cohort of 2344 individuals. The authors report that remdesivir therapy was not associated with improved 30-day survival but was associated with a significant increase in median time to hospital discharge (6 days [interquartile range, 4-12 days] vs 3 days [interquartile range, 1-7 days]; $P < .001$).
- This randomized clinical trial aimed to determine whether oral azithromycin in outpatients with SARS-CoV-2 infection leads to absence of self-reported COVID-19 symptoms at day 14. The study enrolled 263 outpatients remotely via internet-based surveys and followed up participants for 21 days. The authors report that treatment with a single oral dose of azithromycin, 1.2 g, vs placebo resulted in self-reported absence of COVID-19 symptoms at day 14 in 50% vs 50%; this was not statistically significant. Their findings do not support the routine use of azithromycin for outpatient SARS-CoV-2 infection.
- This prospective, open-label, randomised superiority trial among participants enrolled at 19 hospitals in the UK aimed to assess whether azithromycin is effective in preventing hospital admission or death in adult patients with clinically diagnosed COVID-19 infection being managed on an ambulatory care pathway. The primary outcome was assessed in 292 participants (145 in the azithromycin group and 147 in the standard care group). The authors report that 15 (10%) participants in the azithromycin group and 17 (12%) in the standard care group were admitted to hospital or died during the study (adjusted OR 0.91 [95% CI 0.43–1.92], p=0.80). There were no serious adverse events reported. Their findings in mild-to-moderate COVID-19 managed in ambulatory care suggest that azithromycin does not reduce hospital admissions, respiratory failure, or death compared with standard care, and should not be used in the treatment of COVID-19.
- This cohort study investigating SARS-CoV-2 seroprevalence in 55 randomly selected schools in Switzerland (Ciao Corona) compared symptoms compatible with long COVID in children and adolescents reported within 6 months after SARS-CoV-2 serologic testing. Between October and November 2020 and March and April 2021, 4 of 109 seropositive children (4%) vs 28 of 1246 seronegative ones (2%) reported at least 1 symptom lasting beyond 12 weeks. The most frequently reported symptoms lasting more than 12 weeks among seropositive children were tiredness (3/109, 3%), difficulty concentrating (2/109, 2%), and increased need for sleep (2/109, 2%). None of the seropositive children reported hospitalization after October 2020.
- This meta analysis aimed to estimate the association between administration of Interleukin 6 (IL-6) antagonists compared with usual care or placebo and 28-day all-cause mortality and other outcomes. The analysis included 27 clinical trials with a total of 10,930 patients,of whom 2565 died by 28 days. The 28-day all-cause mortality was lower among patients who received IL-6 antagonists compared with those who received usual care or placebo (summary odds ratio, 0.86). The summary odds ratios for the association of IL-6 antagonist treatment with 28-day all-cause mortality were 0.78 with concomitant administration of corticosteroids vs 1.09 without administration of corticosteroids.
- This ongoing phase 3, randomized, double-blind, placebo-controlled trial included a total of 1035 ambulatory patients with mild or moderate COVID-19 who were at high risk for progression to severe disease. The authors randomized the patients in a 1:1 ratio to receive a single intravenous infusion of either a neutralizing monoclonal-antibody combination agent (2800 mg of bamlanivimab and 2800 mg

of etesevimab, administered together) or placebo within 3 days after a laboratory diagnosis of SARS-CoV-2) infection. The authors found that bamlanivimab plus etesevimab led to a lower incidence of COVID-19–related hospitalization and death than did placebo and accelerated the decline in the SARS-CoV-2 viral load.

Epidemiology

- This study analyzed more than 300,000 SARS-CoV-2 genomes available in the Gisaid database as of January 2021 and demonstrates adaptive evolution of the virus that affects, primarily, multiple sites in the spike and nucleocapsid protein. The authors report that selection appears to act on combinations of mutations in these and other SARS-CoV-2 genes. Evolution of the virus is accompanied by ongoing adaptive diversification within and between geographic regions. This diversification could substantially prolong the pandemic and the vaccination campaign, in which variant-specific vaccines are likely to be required.
- This research letter reports on the identification of SARS-CoV-2 RNA in an oropharyngeal swab specimen collected from a child with suspected measles in early December 2019, approximately 3 months before the first identified COVID-19 case in Italy. Their finding is of epidemiologic importance because it expands knowledge on timing and mapping of the SARS-CoV-2 transmission pathways.
- This genomic surveillance study reports on the patterns of SARS-Cov-2 introductions, evolution and spread across six coastal Counties of Kenya (Mombasa, Kilifi, Kwale, Tana River, Taita Taveta and Lamu). The authors analyzed 684 genomes from samples collected during the first two waves (March 2020 - February 2021). They detected up to 32 Pango lineages in the local sample with six accounting for 88.0% of the sequenced infections: B.1 (60.4%), B.1.1 (8.9%), B.1.549 (7.9%), B.1.530 (6.4%), N.8 (4.4%) and A (3.1%). In a contemporaneous global sample, they identified 571 lineages, 247 for Africa and 88 for East Africa. They detected 262 location transition events comprising: 64 viral imports into Coastal Kenya; 26 viral exports from coastal Kenya; and 172 inter-county import/export events. Most international viral imports (61%) and exports (88%) occurred through Mombasa, a key coastal touristic and commercial center; and many occurred prior to June 2020, when stringent local COVID-19 restriction measures were enforced. After this period, local transmission dominated, and distinct local phylogenies were seen. Their analysis supports moving control strategies from a focus on international travel to local transmission. [*not peer reviewed*]
- This modelling study aimed to estimate the impact of the pandemic on global and regional childhood routine immunisation. The authors report that globally, estimated coverage in 2020 fell to 76.7% for DTP3, levels not seen since 2008, while MCV1 dropped to 78.9%, levels not seen since 2006. These COVID-19-related disruptions were most severe in the earlier months of the pandemic, reaching a nadir in April, 2020. The second half of 2020 showed signs of recovery, as global monthly doses administered began nearing expected estimates by December, 2020. Nevertheless, recovery efforts were far from complete, with an additional 8.5 million children still missing DTP3 doses and 8.9 million children still missing MCV1 doses, at the end of 2020. In the absence of concerted routine immunisation catch-up and expansion efforts, especially as populations return to pre-pandemic interactions, the world will face heightened risks of vaccine-preventable diseases in 2021 and beyond.
- This interim analysis of an ongoing observational, prospective cohort study across Western Pennsylvania aimed to assess antibody responses, levels, and neutralization capability after COVID-19 vaccination among immunocompromised patients and compare these to those of immunocompetent healthcare workers. The study enrolled 107 HCW and 489 immunocompromised patients. The authors report that compared to HCWs, seropositivity was significantly lower among immunocompromised patients with solid organ transplant (SOT), autoimmune, hematological malignancies, and solid tumors (HCW=98.1%; SOT=37.2%; autoimmune=83.8%; hematological malignancies=54.7%; and solid tumor=82.4%, $p < 0.05$). Over 94% of patients with HIV were seropositive. Among seropositive patients, antibody levels were lower in SOT patients than healthy controls. [*not peer reviewed*]

- This retrospective analysis of surveillance results obtained from students and employees in a university setting aimed to detect and desribe breakthrough infections. The authors sequenced 2,551 out of 68,428 random surveillance nasal-pharyngeal swabs collected on Purdue University Campus between February and May 2021 from fully vaccinated individuals. The authors found 14 cases of breakthrough infection by Nucleic acid amplification testing (0.55%, 95% CI: 0.30 - 0.92). Many of these breakthroughs were associated with variants of concern (VOCs -B.1.1.7 and P.1). Asymptomatic infections composed 9/14 (64%) of the cases, and the majority of cases were detected in females (10/14, 71%).The single B.1.617.2 (Delta) breakthrough was in a symptomatic female (56-65 years old) previously vaccinated with Ad26.COV2.S (Johnson & Johnson/Janssen) who had three Ct values <18. [*not peer reviewed*]
- This cross-sectional study assessed the gap between excess mortality (EM) and COVID-19 confirmed mortality (CCM) in 67 countries to determine the extent to which official data on COVID-19 deaths might be considered reliable. The authors used negative binomial regression models to estimate projected deaths in 2020 using mortality data from 2015 to 2019. Their results revealed that most of the 67 countries experienced an increase in mortality during 2020. Their comparison revealed the different national health systems' capacity to test and diagnose COVID-19 and their responsiveness to the health crisis. Most of the countries that presented reduced overall mortality during 2020 had extremely high testing capacity and were praised for their effective response measures against the pandemic.
- This cross-sectional study across the 47 prefectures in Japan (with a total population of 126.2 million) aimed to assess the association between regional COVID-19 outcome disparities and socioeconomic characteristics. A total of 412,126 confirmed COVID-19 cases (326.7 per 100 000 people) and 6,910 deaths (5.5 per 100 000 people) were reported as of February 13, 2021. A higher burden of COVID-19 cases and deaths was observed in prefectures with lower household incomes; a higher proportion of the population receiving public assistance; a higher unemployment rate; higher numbers of retail, transportation and postal, and restaurant industry workers; more household crowding; and higher smoking and obesity rates. Their results on the pattern of socioeconomic disparities in COVID-19 outcomes was similar to that observed in the US and Europe.
- This prospective cohort study aimed to compare in-hospital mortality and other patient characteristics between the 1st and 2nd COVID-19 waves in South Africa. The authors analysed data from the DATCOV national active surveillance system from 5th March 2020 to 27th March 2021. Their results showed that peak rates of COVID-19 cases, admissions, and in-hospital deaths in the second wave exceeded rates in the first wave. After adjusting for weekly COVID-19 hospital admissions, there was a 31% increased risk of in-hospital mortality in the second wave (aOR 1.31, 95% CI 1.28–1.35). In-hospital case-fatality risk increased from 17.7% in weeks of low admission (<3500 admissions) to 26.9% in weeks of very high admission (>8000 admissions; aOR 1.24, 1.17–1.32).

Infection Prevention and Control

- This study aimed to investigate a nosocomial outbreak of COVID-19 in a hematologic ward of a tertiary hospital in Seoul, Korea. The authors identified 10 additional COVID-19 cases involving patients with hematologic malignancies and their guardians from the index patient within 6 days of admission after thorough contact tracing and CCTV monitoring. They also performed airflow investigation with a simulation software together with whole genome sequencing of SARS-CoV-2 and identified one patient who had probably acquired COVID-19 through airborne- transmission. The rapid transmission of SARS-CoV-2 in the hematologic ward occurred as a result of the multi-patient room setting, resident caregiver interaction, and shared bathroom, which was triggered by presymptomatic transmission.

Non-pharmaceutical interventions, social distancing

- This modelling study retrospectively examined differences in SARS-CoV-2 transmission and related mortality in care homes, hospitals, and the community in England since the virus was first introduced in December 2020. They found that of the control measures implemented, only national lockdown

brought the reproduction number (R_t^{eff}) below 1 consistently; if introduced 1 week earlier, it could have reduced deaths in the first wave from an estimated 48,600 to 25,600 (95% CI: 15,900 to 38,400).

- This cross-sectional study used a web-based questionnaire to evaluate the usage patterns and consumer perceptions of the effectiveness and health safety of bar soap, liquid hand soap, and hand sanitizer products before and after the spread of COVID-19 among 1000 Koreans. Their results show that the number of consumers who primarily use bar soap has decreased from 71.8 to 51.4%, the number of those who primarily use liquid hand soap has increased from 23.5 to 41.3%, and the number of those who use and carry hand sanitizer has increased. The frequency of use, duration of use, and amount used of all three products have increased significantly since the COVID-19 outbreak. Consumer perception of the products' preventive effect against COVID-19 is higher for liquid hand soap and hand sanitizer than it is for bar soap.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 15th July 2021, Ocugen, a biopharmaceutical company, announced that it had initiated a rolling submission to Health Canada for COVAXIN, a vaccine against COVID-19, which is co-developing with Bharat Biotech International Ltd. This follows after COVAXIN phase 3 clinical trial results demonstrated efficacy and safety in nearly 25,800 adults. COVAXIN is a highly purified and inactivated vaccine that is manufactured using a vero cell manufacturing platform with an excellent safety track record. It is a two-dose vaccine given four weeks apart. COVAXIN is currently being administered under emergency use authorizations in 13 countries, and applications for emergency use authorization are pending in more than 60 additional countries.
- On 14th July 2021, ImmunityBio announced authorization from the South Africa Health Products Regulatory Authority (SAHPRA) to proceed with Phase 1/2/3 randomized trial in South Africa of their dual-Antigen T-Cell vaccine as a universal boost in previously vaccinated populationagainst COVID 19.The phase 1/2/3 clinical study is scheduled to commence in the third quarter of this year. It will study the hAd5 Spike + Nucleocapsid (S+N) as a boost for South African healthcare workers previously vaccinated with a spike-only antibody-based vaccine.
- On 12th July 2021, ReiThera Srl, a biotech company announced the preliminary safety and immunogenicity data from the Phase 2 clinical trial with GRAd-COV2 vaccine candidate. Data shows that the vaccine was well-tolerated and triggered immune responses. The study was conducted in 24 clinical centers in Italy and enrolled 917 volunteers (25% of subjects were >65 years old and/ or with conditions associated with an increased risk of severe disease in case of SARS-CoV-2. Following a recent review of the data, trial's Independent Data Safety Monitoring Board and the Steering Committee (Scientific Committee for the evaluation of efficacy) recommended the continuation of the clinical development of the GRAd-COV2 vaccine.
- On 12th July 2021, NOVAC Biotech Ltd. announced that it had signed an advance purchase agreement (APA) with the Global Alliance for Vaccines and Immunization (Gavi Alliance), which is on behalf of COVAX Facility, to provide up to 380 million doses of inactivated COVID-19 vaccine, CoronaVac for distribution under COVAX Facility. SINOVAC will supply 50 million doses of CoronaVac® by the end of September of 2021. In addition, Gavi has the option to purchase an additional 150 million doses in the fourth quarter of 2021 and 180 million more doses in the first half of 2022. In total, up to 380 million doses of CoronaVac will be available to both self-financing participants of the Facility as well as those supported by the Gavi COVAX AMC.
- On 1st July 2021, Zydus Cadila announced that the company has applied for Emergency Use Authorization (EUA) to the office of Drug Controller General of India (DCGI) for ZyCoV-D, its Plasmid DNA Vaccine against COVID-19. This follows after positive interim results from the Phase III clinical

trial of ZyCoV-D. Data shows that ZyCoV-D is well tolerated and safe for children in the age group of 12 to 18 years. The phase III clinical trial study was conducted in over 50 centers and is considered the largest Covid-19 vaccine study in India.

- On 8th July 2021, Pfizer and BioNTech companies provided information that they are developing an updated version of the Pfizer-BioNTech COVID-19 vaccine that targets the full spike protein of the Delta variant and anticipates to roll out clinical studies in August, subject to regulatory approvals. This comes after initial data from the ongoing booster trial study demonstrates that the third dose of BNT162b2 given 6 months after the second dose has a consistent tolerability profile while eliciting high neutralization titers against the wild type and the Beta variant, which are 5 to 10 times higher than after two primary doses.

Therapeutics trials:

- On 15th July 2021, Corvus Pharmaceuticals announced that it has discontinued its Phase 3 study of mupadolimab for COVID-19 due to positive trends exhibited by COVID-19 vaccines in lowering serious infection and hospitalizations. The discontinuation is not related to any safety or efficacy issues observed in study patients. The Company will continue to advance the development of mupadolimab in oncology, where it is currently being studied in a Phase 1/1b clinical trial.
- On 8th July 2021, a joint research group from Korea Advanced Institute of Science and Technology (KAIST) and Institut Pasteur Korea reported that they had detected repurposed drugs for COVID-19 treatment through virtual screening and cell-based assays. From a pool of 6,218 US Food and Drug Administration-cleared (FDA) therapies or those in the clinic, the team found 38 drugs that can be repurposed to potentially treat Covid-19. Seven of these compounds inhibited SARS-CoV-2 replication in Vero cells. Three of these drugs, emodin, omipalisib, and tipifarnib, showed anti-SARS-CoV-2 activity in human lung cells. Drug repurposing is a practical strategy for developing antiviral drugs in a short period of time, especially during a global pandemic.
- On 7th July 2021, a research team at Queensland University of Technology (QUT) in Australia announced they had discovered a new binding site on the SARS-CoV-2 spike (S) protein, which could be used as a target for anticoagulant drugs. The novel binding site on the N-terminal domain (NTD), is a different area of the virus's spike that facilitates the binding of heparan sulphate (HS). Binding of the CoV-2 spike protein to heparan sulphate (HS) on cell surfaces is generally the first step in a cascade of interactions the virus needs to initiate an infection and enter the cell. Thus, targeting the NTD site with molecules like heparin (or heparin mimetics) is a possible strategy to stop the virus binding to cells and infecting them.Heparin and its mimetics could be used to treat people with severe effects of the virus and any emerging variants. Further findings indicate that molecules that mimic the 3D structure of heparin, might be potential broad-spectrum antiviral drugs for COVID-19 and other emerging viral threats.
- On 6th July 2021, Algernon Pharmaceuticals, announced that it will not be advancing Ifenprodil into a Phase 3 clinical study for COVID-19. The decision was based on several factors including the overall findings of the Phase 2b COVID-19 study final data set, the global rate of vaccinations to date, other COVID-19 drug treatment programs under development, and the projected trial size, costs and timelines needed to successfully complete a Phase 3 trial.

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 was extended; a down arrow indicates PHSMs were loosened/expired. Member States are organized by tiers based on current epidemiological data from 10th to 16th 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	↑	**Libya** imposed multiple new COVID-19 measures to fight the current surge of transmission, including limits on attendance at weddings and funerals, closure of some businesses including cafes, closure of public transportation, and restrictions on services at restaurants. These measures will remain in place for 2 weeks.
Namibia	→	Officials in **Namibia** announced that current measures to address COVID-19 transmission--including nationwide curfews, compulsory mask-wearing, and limits on public gatherings--will be extended an additional 15 days, until 31 July.
South Africa	↑	COVID-19 restrictions in **South Africa** have been extended for an additional 2 weeks. Measures include a ban on public gatherings, a nightly curfew, and the prohibition of alcohol sales.
Tunisia	→	Two states in **Tunisia**--Grand Tunis and Kasserine Governorate--announced an extension of COVID-19 measures until 31 July and 18 July, respectively. Measures include suspension of weekly markets, a nightly curfew, ban on public gatherings, and suspension of religious services.
Zimbabwe	→	Officials in **Zimbabwe** announced the extension of COVID-19 measures--including a nightly curfew, bans on public gatherings, and capacity restrictions on public transportation--for an additional 14 days, during which time the country's vaccination campaign will ramp up, with the goal of vaccinating 1 million people during the same 2-week timeframe.
Tier 3 (Moderate Alert): Daily case incidence per 1M people/day is 20 to <80 and/or positivity rate is 5% to <12%		
Mauritius	↓	**Mauritius** reopened its borders to international travellers, both vaccinated and unvaccinated, as of 15 July. Travellers must have a negative PCR test upon arrival from no longer than 5-7 days prior.
Morocco	↑	**Morocco** announced it will require travellers from France, Spain, and Portugal to quarantine upon arrival (if they are unvaccinated) due to the high circulation of the Delta variant in those locations. **Morocco** also extended the nationwide state of health emergency until 10 August, and banned Eid Al-Adha (to be celebrated 21 July) prayers in mosques.
Rwanda	↑	In Kigali, capital city of **Rwanda**, 8 districts were placed under a 10-day lockdown, during which only essential services (such as food markets and pharmacies) will be permitted to operate. Schools will close during this time, and public transportation will be suspended.

Tier 2 (Low Alert): Daily case incidence per 1M people/day is 5 to <20 and/or positivity rate is 3% to 5%		
Algeria	↓/↑	**Algeria** reopened its border with Niger, which was closed due to COVID-19, in order to restore trade and lessen the economic burden of the pandemic. Travel into and out of Tebessa, a province in **Algeria**, was also restricted, and additional measures--including take-out only at restaurants and closure of public spaces--were implemented in the region to prevent COVID-19 transmission.
Gambia	↑	The Ministry of Health in **The Gambia** announced increased enforcement of measures to prevent COVID-19 (social distancing, wearing a facemask, etc.), including a fine of D1000 for violators.
Madagascar	→	The state of emergency in **Madagascar** was extended by an additional 15 days. Measures include capacity limits on public gatherings, a nightly curfew, and closure of borders.
Tier 1 (Standard Precautions): Daily case incidence per 1M people/day is <5 and/or positivity rate is <3%		
Nigeria	↑	In Lagos, **Nigeria**, officials announced increased enforcement of measures to prevent COVID-19, and warned of fines, imprisonment, and deportation for people who do not comply.

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