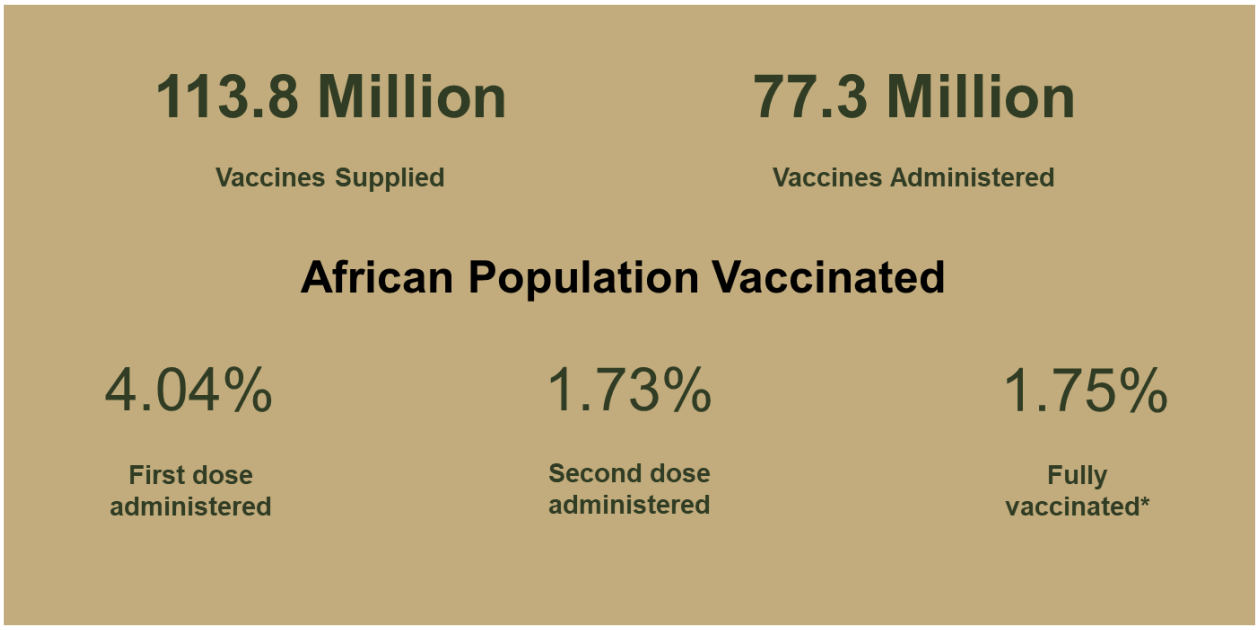
COVID-19 Scientific and Public Health Policy Update[1] – (17 August 2021)

*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

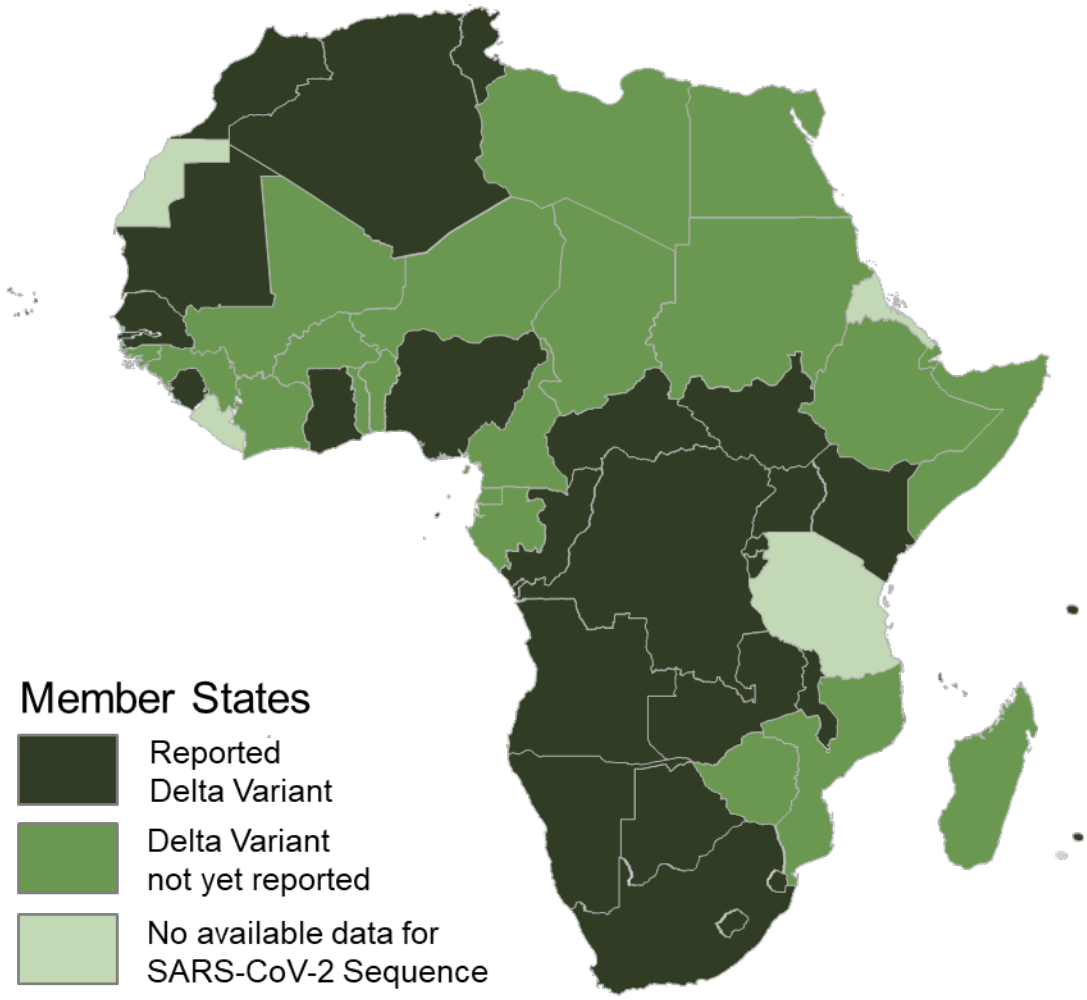


*Received two doses/ one dose of Johnson & Johnson vaccine
https://africacdc.org/covid-19-vaccination/
Updated 11th August 2021

Variants of Concern

- The Delta variant (B.1.617.2), first reported in India, has spread to more than 142 countries worldwide; 28 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 11th August 2021

B. New guidelines and resources

Since 31st July 2021,

- Africa CDC has published new guidance and resources on:
  - Africa announces the rollout of 400m vaccine doses to the African Union Member States and the Caribbean
  - The Critical Role of Community Health Workers in COVID-19 Vaccine Roll Out
- US CDC has published new guidance and resources on:
  - Testing Strategies for SARS-CoV-2
  - Investigating and responding to COVID-19 cases at homeless service provider sites
  - Guidance for Vaccinating Older Adults and People with Disabilities at Vaccination Sites
  - COVID-19 Vaccination Program Operational Guidance
  - Operational Considerations for Community Isolation Centers for COVID-19 in Low-Resource Settings
  - Lab Tests to Collect Shortly After Severe Allergic Reaction/Anaphylaxis Following COVID-19 Vaccination
  - Guidance for COVID-19 Prevention in K-12 Schools
  - Considerations for Case Investigation and Contact Tracing in K-12 Schools and Institutions of Higher Education (IHEs)

- CDC's Interim Guidance for General Population Disaster Shelters During the COVID-19 Pandemic
- WHO has published new guidance and resources on:
  - Guidance for surveillance of SARS-CoV-2 variants
  - Training on handling, storing and transporting Pfizer BioNTech COVID-19 Vaccine COMIRNATY® (Tozinameran)
  - Holding gatherings during the COVID-19 pandemic

- FDA has issued press releases on:
  - FDA authorizes additional vaccine dose for certain Immunocompromised Individuals
  - FDA approved an abbreviated new drug application for dexamethasone sodium phosphate injection.
  - As of 13th August 2021, 402 tests and sample collection devices are authorized by the FDA under emergency use authorizations (EUAs)

- ECDC has issued new resources on:
  - Communicable disease threats report, 8-14 August, week 32

- PHE has issued new guidance and press releases on:
  - Guidance for contacts of people with confirmed coronavirus (COVID-19) infection who do not live with the person
  - Guidance for households with possible coronavirus infection
  - Migrant health guide
  - Evaluating detection of SARS-CoV-2: Antibodies at Home study
  - Management of staff and exposed patients and residents in health and social care settings
  - COVID-19 vaccination: resources for children and young people
  - COVID-19: impacts on health – reports and tools
  - Wider impacts on people aged 65 and over
  - COVID-19 study finds lower prevalence in schools

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 investigated the influence of Bacillus Calmette-Guérin (BCG) vaccination on the unstimulated plasma levels of a wide panel of cytokines, chemokines, acute-phase proteins (APPs), matrix metalloproteinases (MMPs), and growth factors in a group of healthy elderly individuals (age, 60 to 80 years) at baseline (before vaccination) and 1 month after vaccination as part of their clinical study to examine the effect of BCG on COVID-19. Their results demonstrated that BCG vaccination resulted in diminished plasma levels of types 1, 2, and 17 and other pro-inflammatory cytokines and type 1 interferons. BCG vaccination also resulted in decreased plasma levels of CC, CXC chemokines, APPs, MMPs, and growth factors. Plasma levels of the aforementioned parameters were significantly lower in vaccinated individuals when compared to unvaccinated control individuals. Their results demonstrate the immunomodulatory properties of BCG vaccination and suggests its potential utility in nonspecific vaccination of COVID-19 by down-modulating pathogenic inflammatory responses.

- This study demonstrates that convalescent subjects previously infected with ancestral variant SARS-CoV-2 produce antibodies that cross-neutralize emerging SARS-CoV-2 variants of concern (VOCs) with high potency. The authors identified four receptor binding domain (RBD)–targeting antibodies from three early-outbreak convalescent donors with potent neutralizing activity against 23 variants, including the B.1.1.7, B.1.351, P.1, B.1.429, B.1.526, and B.1.617 VOCs. Two antibodies are ultrapotent, with subnanomolar neutralization titers. Structural and functional analyses revealed that antibody breadth is mediated by targeting a site of vulnerability at the RBD tip offset from major mutational hotspots in VOCs. Selective boosting of immune responses targeting specific RBD epitopes, such as the sites defined by these antibodies, may induce breadth against current and future VOCs.
- This study investigated the structural and functional consequences of emerging mutations on neutralizing antibodies (nAbs) isolated from COVID-19 convalescent patients, as well as their effect on angiotensin-converting enzyme 2 (ACE2) receptor binding. Receptor binding site (RBS) residues Glu^{484}, Lys^{417}, and Asn^{501} are mutated in variants first described in South Africa (B.1.351) and Brazil (P.1). The authors analyzed their effects on angiotensin-converting enzyme 2 binding, as well as the effects of two of these mutations (K417N and E484K) on nAbs isolated from COVID-19 patients. Binding and neutralization of the two most frequently elicited antibody families (IGHV3-53/3-66 and IGHV1-2), which can both bind the RBS in alternative binding modes, are abrogated by K417N, E484K, or both. These effects can be structurally explained by their extensive interactions with RBS nAbs. However, nAbs to the more conserved, cross-neutralizing CR3022 and S309 sites were largely unaffected. Their results have implications for next-generation vaccines and antibody therapies.
- In this study, the authors developed a protein subunit vaccine composed of spike ectodomain protein (StriFK) plus a nitrogen bisphosphonate–modified zinc-aluminum hybrid adjuvant (FH002C). StriFK-FH002C generated substantially higher neutralizing antibody titers in 3 animal models (mice, hamsters, and cynomolgus monkeys) than those observed in plasma isolated from COVID-19 convalescent individuals. StriFK-FH002C also induced both T_H1- and T_H2-polarized helper T cell responses in mice. In hamsters, StriFK-FH002C immunization protected animals against SARS-CoV-2 challenge, as shown by the absence of virus-induced weight loss, fewer symptoms of disease, and reduced lung pathology. Vaccination of hamsters with StriFK-FH002C also reduced within-cage virus transmission to unvaccinated, cohoused hamsters. StriFK-FH002C represents an effective, protein subunit–based SARS-CoV-2 vaccine candidate.
- This ex vivo study investigated whether prior Measles-Mumps-Rubella (MMR) or Tetanus-Diphtheria-Pertussis (Tdap) vaccination elicit cross-reactive T cells that mitigate COVID-19. The authors observed high correlation between T cell responses to SARS-CoV-2 (Spike-S1 and Nucleocapsid) and MMR and Tdap proteins in COVID-19 convalescent and vaccinated individuals. The overlapping T cell population contained an effector memory T cell subset (TEMRA) implicated in protective, anti-viral immunity and their detection required APC-derived IL-15, known to sensitize T cells to activation. Cross-reactive T Cell Receptor (TCR) repertoires detected in antigen-experienced T cells recognizing SARS-CoV-2, MMR and Tdap epitopes had TEMRA features. Indices of disease severity were reduced in MMR or Tdap vaccinated individuals by 32-38% and 20-23% respectively, among COVID-19 patients.
- This study aimed to investigate whether intranasally (IN) administered ChAdOx1 nCoV-19 reduces detection of virus in nasal swabs in 2 animal models. The authors challenged vaccinated macaques and hamsters with SARS-CoV-2 carrying a D614G mutation in the spike protein. Their findings show that IN vaccination of hamsters and non-human primates (NHPs) with ChAdOx1 nCoV-19 resulted in a robust mucosal and humoral immune response. When compared to hamsters vaccinated via the IM route, a reduction in virus load in swabs was found in IN vaccinated animals, combined with full protection of the respiratory tract (no viral RNA). In NHPs, they observed a reduction in infectious virus

in swabs at 1 day post infection ($p < 0.05$). Viral load in bronchoalveolar lavage and the lower respiratory tract were reduced, and they were unable to find any signs of pneumonia in vaccinated hamsters or NHPs. Their findings warrant further investigation on intranasal delivery of COVID-19 vaccines.

- In this review, the authors provide an overview of the COVID-19 pathogenesis in various organ systems, the overall advantages of cell therapies, potential cell targets and strategies within each organ system, and a summary of current cell therapy studies and trials for COVID-19 as of 1 January 2021.

Vaccines

- This matched test-negative, case-control study aimed to assess real-world effectiveness of the BNT162b2 and mRNA-1273 vaccines against the SARS-CoV-2 Delta (B.1.617.2) variant in the population of Qatar. The authors found that BNT162b2 effectiveness against any Delta infection, symptomatic or asymptomatic, was 64.2% (95% CI: 38.1-80.1%) ≥14 days after the first dose and before the second dose, but was only 53.5% (95% CI: 43.9-61.4%) ≥14 days after the second dose. Corresponding effectiveness measures for mRNA-1273 were 79.0% (95% CI: 58.9-90.1%) and 84.8% (95% CI: 75.9-90.8%), respectively. Effectiveness against any severe, critical, or fatal COVID-19 disease due to Delta was 89.7% (95% CI: 61.0-98.1%) for BNT162b2 and 100.0% (95% CI: 41.2-100.0%) for mRNA-1273, ≥14 days after the second dose. Both vaccines are highly effective in preventing Delta hospitalization and death, but less so in preventing infection, particularly for BNT162b2. [*not peer reviewed*]
- This ongoing phase 2-3, observer-blinded, placebo-controlled trial aimed to evaluate the safety, immunogenicity, and efficacy of mRNA-1273 in adolescents between the ages of 12 and 17 years of age. The authors randomly assigned 3732 healthy adolescents in a 2:1 ratio to receive two injections of the mRNA-1273 vaccine (2489 participants) or placebo (1243 participants), administered 28 days apart. In the mRNA-1273 group, the most common solicited adverse reactions after the first or second injections were injection-site pain (in 93.1% and 92.4%, respectively), headache (in 44.6% and 70.2%, respectively), and fatigue (in 47.9% and 67.8%, respectively); in the placebo group, the most common solicited adverse reactions after the first or second injections were injection-site pain (in 34.8% or 30.3%, respectively), headache (in 38.5% and 30.2%, respectively), and fatigue (in 36.6% and 28.9%, respectively). No serious adverse events related to mRNA-1273 or placebo were noted. The mRNA-1273 vaccine had an acceptable safety profile in adolescents. The immune response was similar to that in young adults, and the vaccine was efficacious in preventing COVID-19.
- This study assessed three SARS-CoV-2 antibody markers (IgG bAbs to Spike, IgG bAbs to Spike RBD, ID50 nAb titer), as well as 80% inhibitory dilution (ID80) nAb titer, as correlates of risk of COVID-19 and as correlates of mRNA-1273 vaccine protection against COVID-19 in the COVE trial. Through case-cohort sampling, participants were selected for measurement of the 4 serum antibody markers at Day 1 (1st dose), Day 29 (2nd dose), and Day 57. The authors report that for recipients of two doses of mRNA-1273 in the COVE trial, all four antibody markers at Day 29 and at Day 57 were inverse correlates of risk of COVID-19 occurrence through 3-4 months post second dose. Based on any of the antibody markers, COVID-19 risk was about 10 times lower for vaccine recipients with antibodies in the top 10% of values compared to those with negative/undetectable values (the same value as in baseline negative placebo recipients). [*not peer reviewed*]
- This vaccine booster study aimed to evaluate immune persistence of two priming doses of CoronaVac, and immunogenicity and safety of a third dose in healthy adults ≥60 years. The authors examined neutralizing antibody titres six months or more after the second dose in all participants and provided a

third dose to 303 participants recruited in phase 2 trial to assess their immune responses. They found that neutralizing antibody titres declined substantially six months after two doses of CoronaVac among older adults. A third dose given 8 months or more after the second dose significantly increased neutralizing antibody levels. These findings could help policymakers determine the necessity and the timing of a booster dose for older adults. [*not peer reviewed*]

- This participant-blinded, randomised, phase 2, UK multicentre trial aimed to determine whether the immune responses to heterologous schedules with the ChAdOx1 nCoV-19 (ChAd) and BNT162b2 (BNT) vaccines are non-inferior to their equivalent homologous schedules. Majority of the eligible participants in the Com-COV trial were enrolled into the general cohort (28-day or 84-day prime-boost intervals), who were randomly assigned (1:1:1:1:1:1:1:1) to receive ChAd/ChAd, ChAd/BNT, BNT/BNT, or BNT/ChAd, administered at either 28-day or 84-day prime-boost intervals. This article reports on the results from 463 participants with a 28-day prime-boost interval. The mean age of participants was 57.8 years (SD 4.7), with 212 (46%) female participants and 117 (25%) from ethnic minorities. At day 28 post boost, the geometric mean concentration of SARS-CoV-2 anti-spike IgG in ChAd/BNT recipients (12,906 ELU/mL) was non-inferior to that in ChAd/ChAd recipients (1392 ELU/mL), with a GMR of 9.2 (one-sided 97.5% CI 7.5 to ∞). In participants primed with BNT, the authors did not show non-inferiority of the heterologous schedule (BNT/ChAd, 7,133 ELU/mL) against the homologous schedule (BNT/BNT, 14,080 ELU/mL), with a GMR of 0.51 (one-sided 97.5% CI 0.43 to ∞). Four serious adverse events occurred across all groups, none of which were considered to be related to immunisation. Their findings support flexibility in the use of heterologous prime-boost vaccination using ChAd and BNT COVID-19 vaccines.
- This phase 2, prospective, randomised, double-blind, placebo-controlled, and multi-centre study aimed to evaluate the safety, tolerability, and immunogenicity of the SARS-CoV-2 vaccine candidate MVC-COV1901, a recombinant protein vaccine containing prefusion-stabilized spike protein S-2P adjuvanted with CpG 1018 and aluminium hydroxide. The study comprised 3,844 participants of ≥ 20 years, who were generally healthy or with stable pre-existing medical conditions, who were randomly assigned in a 6:1 ratio to receive either MVC-COV1901 containing 15 µg of S-2P protein or placebo containing saline. Participants received two doses of MVC-COV1901 or placebo, administered 28 days apart via intramuscular injection. The authors report that no vaccine-related Serious Adverse Events (SAEs) were recorded. The most common solicited adverse events across all study participants were pain at the injection site (64%), and malaise/fatigue (35%). Fever was rarely reported (<1%). For all participants in the MVC-COV1901 group, at 28 days after the second dose against wild type SARS-CoV-2 virus, the GMT was 662.3 (408 IU/mL), the GMT ratio was 163.2, and the seroconversion rate was 99.8%. Their result supports MVC-COV1901 to enter phase 3 efficacy trials. [*not peer reviewed*]
- This double-blind, randomized, controlled trial among 120 organ-transplant recipients aimed to assess the safety and immune response of a third dose of mRNA-1273 vaccine. The participants who had received two doses of mRNA-1273 were randomly assigned in a 1:1 ratio to receive either a third dose of mRNA-1273 vaccine or saline placebo 2 months after the second dose of mRNA-1273 (dosing schedule: 0, 1, and 3 months). The authors report that at month 4, an anti-RBD antibody level of at least 100 U per milliliter was present in 33 of 60 patients (55%) in the mRNA-1273 group and in 10 of 57 patients (18%) in the placebo group (relative risk, 3.1; 95% CI, 1.7 to 5.8; P<0.001). After the third dose, the median percent virus neutralization was 71% in the mRNA-1273 group and 13% in the placebo group (95% CI for the between-group difference, 11 to 76 percentage points), and the percentage of patients above the 30% threshold for neutralizing antibody positivity was 60% and 25%, respectively (relative risk, 2.4; 95% CI, 1.5 to 4.0).

- This prospective cohort study aimed to characterise the levels of specific SARS-CoV-2 antibodies in the breast milk of mRNA-vaccinated women across time, as well as their correlation with serum antibody levels. The study included 33 participants. The authors collected serum and breast milk samples simultaneously from each participant at 3 time points: 2 weeks after receiving the first dose of the vaccine (time point 1), 2 weeks after receiving the second dose (time point 2), and 4 weeks after the second dose (time point 3). Their results suggest that breast milk from women vaccinated with the novel mRNA-based Pfizer-BioNTech vaccine contains specific anti–SARS-CoV-2 IgG (S1) antibodies. They also found that after the second dose, breast milk IgG (S1) levels increased and were positively associated with corresponding serum levels.

Diagnostics

- This study describes a rapid and quantitative detection method of anti-SARS-CoV-2 IgG antibody that was built based on the optofluidic point-of-care testing fluorescence (OPOCT) biosensor. The portable system is suitable for on-site sensitive determination of anti-SARS-CoV-2 IgG antibody in total serum without dilution. The whole detection procedure is about 25 min with a detection limit of 12.5 ng/mL (comparable to other immunoassay for IgG detection). IgM and other components in serum had no significant effects on IgG detection. Compared to ELISA test results, their proposed method exhibits several advantages including wider measurement range and easier operation.
- This study describes the development of a paper-based device to detect nucleic acids of pathogens of interest in complex samples using loop-mediated isothermal amplification (LAMP) by producing a colorimetric response visible to the human eye. The authors developed and optimized the device to detect SARS-CoV-2 in human saliva without preprocessing. Their device was capable of detecting the virus within 60 min and had an analytical sensitivity of 97% and a specificity of 100% with a limit of detection of 200 genomic copies/µL of patient saliva using image analysis. The estimated cost per test is ~$10.
- This prospective, longitudinal study aimed to investigate the testing timeframe that optimizes saliva sensitivity for SARS-CoV-2 detection. The authors tested 889 paired nasopharyngeal swab-saliva samples from 404 participants, of which SARS-CoV-2 was detected in 524 nasopharyngeal (58.9%) and 318 saliva (35.7%) specimens. SARS-CoV-2 was detected in both specimens in 258 pairs (29.0%). Saliva was sensitive for detecting SARS-CoV-2 in symptomatic individuals during initial weeks of infection, but sensitivity in asymptomatic SARS-CoV-2 carriers was less than 60% at all time points. The authors suggest saliva-based RT-PCR should not be used for asymptomatic COVID-19 screening.

Care and Treatment

- This open-label, adaptive, multiplatform, controlled trial, among hospitalized patients with COVID-19 who are not critically ill, aimed to determine whether an initial strategy of therapeutic-dose anticoagulation with unfractionated or low-molecular-weight heparin improves in-hospital survival and reduces the duration of ICU-level cardiovascular or respiratory organ support. The final analysis included 2219 patients. The probability that therapeutic-dose anticoagulation increased organ support–free days as compared with usual-care thromboprophylaxis was 98.6% (AOR, 1.27; 95% CI, 1.03 to 1.58). The adjusted absolute between-group difference in survival until hospital discharge without organ support favoring therapeutic-dose anticoagulation was 4.0 percentage points (95% CI, 0.5 to 7.2). In non-critically ill patients with COVID-19, an initial strategy of therapeutic-dose anticoagulation with heparin increased the probability of survival until hospital discharge with reduced use of ICU-level organ support as compared with usual-care thromboprophylaxis.
- This longitudinal study aimed to determine the clinical presentation of COVID-19 and risk factors for COVID-19 mortality among diabetic patients. The authors reviewed case records of COVID-19 patients

with admitted for treatment from June 2020 to September 2020 in a tertiary care hospital in South India. They found that 23% (200) of the COVID-19 patients admitted in the hospital had diabetes. Fever (59.5%), cough (48%), difficulty in breathing (42%) and myalgia (26.5%) are the common symptoms among diabetic COVID-19 patients. The median survival time was slightly lesser in male COVID-19 patients (15 days) as compared to female patients (16 days). The risk of mortality among COVID-19 patients with diabetes is increased for patients who presented with breathlessness (aRR=4.5 (95% CI: 2.3-8.8)), had positive history of smoking (aRR=1.9 (95% CI: 1.1-3.8)), who had Chronic Kidney Disease (aRR=1.8 (95% CI: 1.1-2.8)) and who had cardiac illness (aRR=1.6 (95% CI: 0.9-2.7)).

- This retrospective study at an urban academic U.S hospital aimed to compare laboratory findings among pregnant patients with severe acute respiratory syndrome coronavirus (SARS-CoV-2) by symptom status and disease severity. The authors identified 175 pregnant patients with SARS-CoV-2, of whom 100 (57%) were symptomatic; 17 (17%) of those who were symptomatic had severe to critical disease. Compared to asymptomatic people, symptomatic people were more likely to exhibit elevated high sensitivity C-reactive protein (hsCRP) after adjusting for gestational age (aOR 5.67, 95% CI 1.42-22.52, sensitivity 81%, specificity 43%). In symptomatic individuals, transaminitis (aOR 5.67, 95% CI 1.27-25.43), elevated procalcitonin (PCT) (aOR 16.60, 95% CI 2.61-105.46), and elevated Lactate dehydrogenase (LDH) (aOR 17.55, 95% CI 2.51-122.78) were independently associated with severe to critical disease compared to mild to moderate disease after adjusting for maternal age and obesity. Sensitivity for transaminitis, PCT elevation and LDH elevation was 47%, 87% and 53%, while specificity was 89%, 63% and 90%, respectively, for differentiating disease severity.
- This retrospective cohort study aimed to determine the feasibility and safety of a multisite remote patient monitoring (RPM) program for management of acute COVID-19 illness. The authors leveraged established technology, operational infrastructure, and nursing resources to develop a program for ambulatory management of patients with COVID-19. The program included two care-delivery models with different monitoring capabilities supporting variable levels of patient risk for severe illness. They report an evaluation of 7074 patients served by the program across 41 US states. Among all patients, the RPM technology engagement rate was 78.9%. Rates of emergency department visit and hospitalization within 30 days of enrollment were 11.4% and 9.4%, respectively, and the 30-day mortality rate was 0.4%. Their results imply that a multisite RPM program for management of acute COVID-19 illness is feasible, safe, and associated with a low mortality rate. They recommend further research and expansion of the RPM programs for ambulatory management of other acute illnesses.
- This article reports the results of a single arm phase II study using ruxolitinib (an inhibitor of janus-kinases 1 and 2) in patients with COVID-19 induced acute respiratory distress syndrome (ARDS) requiring mechanical ventilation. Ruxolitinib treatment was well tolerated and 13 (81%) patients survived at least the first 28 days on treatment, which was the primary endpoint of the trial. Immediate start of ruxolitinib after deterioration was associated with improved outcome, as was a lymphocyte-to-neutrophils ratio above 0.07. Treatment with the janus-kinase inhibitor ruxolitinib may be an effective drug in COVID-19 ARDS patients; however, a randomized clinical trial is mandatory to prove this.
- This multi-center, adaptive, randomized, platform trial aimed to evaluate the efficacy of repurposed treatment for COVID-19. The authors report that Fluvoxamine, a selective serotonin reuptake inhibitor (SSRI) commonly used for depression, has shown promising results. The Fluvoxamine group had a lower risk of events (emergency room visits or hospitalisation) compared to the placebo group (RR: 0.65, 95%CI: 0.48,0.87) [*preliminary results*]

Epidemiology

- This prospective case-ascertained study aimed to describe the epidemiologic parameters and analyze the secondary attack rate (SAR) in Antananarivo, Madagascar. The study was conducted from March to June 2020 and included all identified close contacts of laboratory-confirmed COVID-19 infections. The authors included 96 index cases and 179 household contacts. The incubation period (adjusted with the best-fit normal distribution) was found to be 4.1 days (95% CI 0.7–7.5]). The serial interval was 6.0 days (95% CI [2.4–9.6]) after adjusting with the best-fit Weibull distribution. On average, each index case infected 1.6 family members (95%CI [0.9–2.3]). The mean SAR among close contacts was 38.8% (95% CI [19.5–58.2]) with the best-fit gamma distribution. Contacts older than 35 years old were more likely to be infected, and the highest SAR was found among them. Their results provide key insights into the epidemiology of the first wave of SARS-CoV-2 in Madagascar.
- This retrospective cohort study aimed to examine characteristics and outcomes of a large US cohort of women who underwent childbirth with vs without COVID-19. The study involved 869,079 adult women, including 18,715 women with COVID-19, who underwent childbirth at 499 US medical centers between March 1, 2020, and February 28, 2021. The study found that women with COVID-19 giving birth had higher rates of mortality, intubation, ICU admission, and preterm birth than women without COVID-19.
- This cohort study used linked population-based birth registry, laboratory, and public health case data to describe SARS-CoV-2 testing outcomes among infants born during the COVID-19 pandemic and their mothers in Ontario, Canada. The study included 96,689 infants, of which 6,176 (6.4%) had a record of receiving a diagnostic test for SARS-CoV-2; 1724 (1.8%) were tested perinatally (i.e., within the first 2 weeks of life). Only 177 infants (0.1% of births; 2.9% of those tested) were positive for SARS-CoV-2. Of 177 infants infected with SARS-CoV-2, 90 (50.9%) had mothers who tested positive for SARS-CoV-2 at some point during the pandemic; however, only 6 (3.4%) were perinatal cases. Only 156 of 82,484 delivering mothers (0.2%) were known to be positive for SARS-CoV-2 infection within 2 weeks of delivery. The findings of this cohort study provide further evidence suggesting that perinatal transmission of, and early-life infection with, SARS-CoV-2 is rare.
- This self-controlled case series (SCCS) and matched cohort study aimed to quantify the risk of acute myocardial infarction and ischemic stroke associated with COVID-19 by analyzing all COVID-19 cases in Sweden. A total of 86,742 patients with COVID-19 were included in the SCCS study, and 348,481 matched control individuals were also included in the matched cohort study. When day of exposure was included in the risk period, the IRR for acute myocardial infarction was 8.44 (5.45–13.08) for the 1st week, 2.56 (1.31–5.01) for the 2nd week, and 1.62 (0.85–3.09) for weeks 3 and 4 following COVID-19. The corresponding IRRs for ischemic stroke were 6.18 (4.06–9.42) for the 1st week, 2.85 (1.64–4.97) for the 2nd week, and 2.14 (1.36–3.38) for weeks 3 and 4 following COVID-19. In the matched cohort analysis excluding day 0, the odds ratio (OR) for acute myocardial infarction was 3.41 (1.58–7.36) and for stroke was 3.63 (1.69–7.80) in the 2 weeks following COVID-19. When day 0 was included in the matched cohort study, the OR for acute myocardial infarction was 6.61 (3.56–12.20) and for ischemic stroke was 6.74 (3.71–12.20) in the 2 weeks following COVID-19. Their findings suggest that COVID-19 is a risk factor for acute myocardial infarction and ischemic stroke, and highlights the need for vaccination against COVID-19.
- This study acquired and linked publicly available daily data on fine particulate matter ($PM_{2.5}$), the number of COVID-19 cases and deaths, and other confounders for 92 western U.S. counties that were affected by the 2020 wildfires. The authors estimated the association between daily changes in levels of $PM_{2.5}$ and the percentage increase in COVID-19 cases and deaths for the counties in the western United States that were affected by the 2020 wildfires. They also estimated the percentage of the total

number of COVID-19 cases and deaths that were attributable to exposure to high levels of $PM_{2.5}$ during the wildfires for each of the counties.

- This cross-sectional study aimed to identify the common factors of COVID-19 cases and deaths among the 50 most affected countries. The authors performed ordinary least square statistics among a wide range of socio-economic, environmental, climatic and health indicators to explain the number of cases and deaths. Their findings are: (i) obesity is the only significant global denominator for the number of COVID-19 cases and deaths; (ii) the percentage of the population over the age of 65 and number of hospital beds per 1000 population inversely correlated to mortality from COVID-19.

Infection Prevention and Control

- This qualitative study aimed to explore the representations of hand hygiene among health professionals, and the psychosocial barriers and facilitators associated to the use of alcohol-based hand rub (ABHR), to obtain a better understanding of ABHR, healthcare-associated infections (HCAIs), hand hygiene (HH) issues, and to develop adapted educational tools to promote HH. The authors conducted interviews and focused group discussions among 46 healthcare professionals in France. The interviewed identified several barriers and facilitators related to the composition and characteristics of hydro-alcoholic solutions (unpleasantness, harmfulness, and personal preferences for other hand hygiene products), personal factors (work habits, cognitive bias, lack of knowledge and communication) and organizational (professional constraints, product accessibility, financial resources).
- This retrospective cohort study aimed to determine occupational exposures to SARS-CoV-2 and secondary cases among healthcare personnel (HCP) at a large health system. Their findings indicate that transmission of COVID-19 to HCP is low, especially with close adherence to personal protective equipment (PPE) guidelines, but lapses in infection prevention practices, including dining together and omitting eye protection during patient care, especially at times when COVID-19 is circulating widely in the community increase the risk of exposure and subsequent transmission to HCP. Close adherence to infection prevention guidelines is crucial to safely care for patients with COVID-19 and to prevent virus transmission among healthcare workers.

Non-pharmaceutical interventions, social distancing

- This study aimed to investigate whether differences in institutional quality and social capital are correlated with the efficacy of lockdown measures. Their results suggest that both local social capital and institutional quality have affected the efficiency of lockdown measures in Italian provinces. The provinces with greater institutional quality and social capital have better lockdown efficacy; After 30 days of lockdown, the difference in effectiveness due to better institutional quality is more than threefold. In order to boost policy effectiveness, policy makers should invest in long-term policies aimed at changing institutional factors.
- This study aimed to evaluate the impacts of physical distancing policy stringency and residents' compliance on time-varying reproduction number (Rt) in 17 countries. Their results showed that Rt initially surged rapidly, then declined gradually depending on policy stringency. The highest mean policy stringency scores were for Italy and South Korea. Variations in stringency scores were higher in Europe, the US and Australia than in Asia. The human mobility reduction was greater in countries with strict policies. In terms of immediate (0-day lag) effects, Rt reductions were found for workplace-closure, limited-gathering, and stay-at-home policies. At a 7-day lag, Rt reductions were found for workplace closure, restrictions on gatherings, stay-at-home requirements, international travel controls,

contact tracing and reducing walking around. At a 14-day lag, Rt reductions were found for restrictions on gatherings, less visiting and staying in parks, and reduced walking around.

- This ecological study based on time series analysis aimed at analyzing the impact of social distancing policies and subsequent mandatory masking, in the community, on the incidence and effective reproductive number of COVID-19 cases in São Paulo State, Brazil. Their results show that the effectiveness was greater for social distancing (1st intervention), with some incremental impact of mandatory use of face masks. Their findings may reflect either a small impact of face masking or the loosening of social distancing after mandatory use of masks.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 13th August 2021, Moderna Inc. announced that the U.S. Food and Drug Administration (FDA) has approved an update to the emergency use authorization for the Moderna COVID-19 vaccine (mRNA-1273) to include a third dose for immunocompromised individuals 18 years of age or older in the United States. The additional dose is particularly intended for solid organ transplant recipients or those who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise. This decision came after a recent double-blind, randomized controlled trial of 120 individuals who had undergone solid organ transplant procedures (heart, kidney, kidney-pancreas, liver, lung, pancreas) demonstrated that a third dose of the Moderna COVID-19 vaccine improved immune response compared to placebo. In the study, the third dose of mRNA-1273 was generally well tolerated.
- On 11th August 2021, Valneva SE announced the initiation of a further Phase 3 trial (VLA2001-304) for its inactivated, adjuvanted COVID-19 vaccine candidate, VLA2001 in New Zealand. Phase 3 trial aims to generate data in the elderly and is also designed to potentially enable variant-bridging through immune-comparability. It will involve two cohorts. Cohort 1 will enroll about 150 volunteers aged >56 years to generate safety and immunogenicity data. Cohort 2 will compare immunogenicity data of VLA2001, against another COVID-19 vaccine candidate, VLA2101, on variant strains in approximately 600 volunteers aged >12 years. In both cohorts, vaccinations will be administered in a 2-dose immunization scheduled 28 days apart. The trial will be conducted at about 10 trial sites in New Zealand. Clinical trial registration # : NCT04956224
- On 10th August 2021, National Institutes of Health (NIH) reported that it has begun a pilot study to assess the antibody response to a third dose of an authorized COVID-19 mRNA vaccine in kidney transplant recipients who did not respond to two doses of Moderna or Pfizer-BioNTech COVID-19 vaccine. The pilot study, which is called COVID Protection After Transplant (CPAT), is being conducted at Johns Hopkins University in Baltimore and will involve up to 200 adults ages >18 years who had received a kidney transplant a year or more prior to enrolment and have had no recent organ rejection or change in immunosuppression. It aims to determine whether a third dose of one of the mRNA COVID-19 vaccines could confer protection and also to identify characteristics that could help distinguish those kidney transplant recipients who would benefit from a third dose of an mRNA vaccine from those who will require a different approach to achieve protection. Clinical trial registration # : NCT04969263
- On 9th August 2021, INOVIO announced that it has received regulatory allowance from China's Center for Drug Evaluation of the National Medical Products Administration to conduct two clinical trials investigating heterologous boosting of its DNA vaccine candidate for COVID-19, INO-4800. The two studies will evaluate the safety, tolerability and immunogenicity of heterologous prime-boost sequential immunizations using a mixed regimen of INO-4800 and CoronaVac®. Both studies will be conducted in China and will involve healthy adult subjects 18 years of age or older. The trials will be conducted in partnership with Sinovac Biotechnology under the sponsorship of Advaccine Biopharmaceuticals Suzhou and anticipated to begin in the coming months.

- On 5th August 2021, Akston Biosciences Corporation announced that the first participants have been dosed with its protein subunit COVID-19 vaccine candidate, AKS-452 in a Phase II open-label trial in the Netherlands. Phase II trial aims to determine safety, tolerability, and immune response of AKS-452 in nearly 52 healthy participants aged between 18 and 85 years at University Medical Center Groningen (UMCG). Participants will receive either one dose of 90 micrograms or two doses of 45 micrograms 28 days apart. Data readout from the trial is anticipated in the third quarter of this year. Clinical trial registration # : NCT04681092
- On 4th August 2021, the Russian Direct Investment Fund (RDIF) announced the initial safety results of the randomized, single-blind study for the evaluation of the immune response and safety of heterogeneous regimens combining Russian Sputnik Light vaccine and vaccines produced by AstraZeneca, Sinopharm and Moderna in the Buenos Aires province in Argentina. Data of 121 volunteers corresponding to the Sputnik V combination groups demonstrates that both the combination of Sputnik Light with other vaccines and vaccination with two injections of only Sputnik Light shows high safety profile with no serious adverse events related to vaccination.
- On 3rd August 2021, the United Kingdom launched a new largest clinical trial to determine the best interval between Covid-19 vaccine doses for pregnant women in the country. A total of more than 600 pregnant women will be vaccinated as part of the trial and followed up by healthcare professionals throughout pregnancy and after childbirth. Preg-CoV will enrol over 600 subjects aged between 18 and 44 years who are 13 to 34 weeks pregnant and have no other health concerns. The Preg-CoV study will provide vital clinical trial data on the immune response to vaccination at different dose intervals: either 4 to 6 weeks or 8 to 12 weeks. The study is £7.5m financially backed by the government and is led by St George's, University of London. Clinical trial registration # : NCT04754594
- On 20th July 2021, the Coalition for Epidemic Preparedness Innovations (CEPI) and the International Vaccine Institute (IVI) announced a new programme of clinical research which aims to expand access to COVID-19 vaccines in Africa. CEPI will provide funding of up to $12.7m to the Expanding Access and Delivery of COVID-19 Vaccines in Africa (ECOVA) consortium to carry out clinical trials of Sinopharm's BBIBP-CorV vaccine in the African continent. Up to 170 million doses of BBIBP-CorV will be distributed through COVAX Facility. ECOVA will conduct a phase 3, individually randomized, observer-blind, controlled (influenza vaccine) trial to evaluate the safety and efficacy of the BBIBP-CorV (Sinopharm) vaccine against any SARS-CoV- 2 infection among adults 18 years and older. Further, a separate Phase 2 mix and match trial will evaluate the safety and immunogenicity of mixed schedules of BBIBP-CorV and AstraZeneca's COVID-19 vaccine. The trials are expected to begin in September and interim results anticipated by the end of the year. Clinical trial registration # : NCT04984408.

Therapeutics trials:

- On 12th August 2021, AzurRx BioPharma, Inc. announced that it has completed enrolment of subjects into Part 1 of its ongoing RESERVOIR Phase 2 clinical trial that is evaluating niclosamide oral tablet (FW-1022) as a treatment for COVID-19-related gastrointestinal (GI) infections. The Phase 2 RESERVOIR clinical trial is a two-part, two-arm, placebo-controlled study examining the safety of niclosamide in treating patients with COVID-19 GI infections in Part 1 and efficacy of niclosamide in clearing SARS-CoV-2 (SARS2) virus from the GI tract in Part 2. In the part 1 of the trial, about 9 to 18 patients with COVID-19 and GI positive stools for SARS2 will be treated with niclosamide for 14 days and observed closely for any signs of safety issues. Patients aged 18 years and above will be enrolled. After a review by a Data Monitoring Committee shows that niclosamide is well-tolerated, the trial will move on to Part 2. Clinical trial registration # : NCT04858425
- On 11th August 2021, I-Mab reported positive interim data from its phase 2/3 study of plonmarlimab drug (TJM2 or TJ003234) for the treatment of cytokine release syndrome (CRS) in patients with severe COVID-19 in the United States. According to the interim results data, nearly 83.6% of subjects in the plonmarlimab arm had a higher mechanical ventilation free rate compared to 76.7% in the placebo by day 30. Furthermore, the drug lowered mortality rate, with 4.9% and 13.3% noted in the plonmarlimab

and placebo arms, respectively, by day 30. Subjects receiving plonmarlimab had higher recovery rates (68.9% vs 56.7% at day 14 and 80.3% vs 70.0% at day 30) compared to placebo. This double-blind, placebo-controlled, randomised Phase 2/3 trial aims to determine the safety, efficacy and effects on cytokine levels following a single dose of 6 mg/kg of plonmarlimab or placebo in patients with severe COVID-19. Clinical trial registration # : NCT04341116

- On 5th August 2021, Brii Biosciences Limited announced that it has completed enrolment for Phase 3 portion of the ACTIV-2 study evaluating safety and efficacy of combination therapy, BRII-196 plus BRII-198, for Covid-19. BRII-196 and BRII-198 are non-competing SARS-CoV-2 monoclonal neutralizing antibodies derived from convalesce COVID-19 patients. A total of 846 participants with symptomatic Covid-19 who are at high risk of clinical progression have been enrolled from sites in the United States, Brazil, South Africa, Mexico and Argentina. The participants enrolled are being evaluated for the combined primary endpoint of hospitalizations and death, relative to placebo, in the 28 days following treatment. Clinical trial registration # : NCT04501978
- On 4th August 2021, National Institutes of Health reported that full-dose blood thinners decreased the organ support requirements and improved the chances of hospital discharge in moderately ill Covid-19 patients in a large, global clinical trial. Final data analysis of 1,098 critically ill and 2,219 moderately ill patients indicated that the likelihood of full-dose heparin to reduce the need for organ support compared to those who received low-dose heparin was 99% among moderately ill patients at 21 day after enrolment. For critically ill patients, full-dose heparin also decreased the number of major thrombotic events, but it did not reduce the need for organ support or boosted their chances of hospital discharge early after receiving treatment. Clinical trial registration # : NCT04372589
- On 3rd August 2021, Eli Lilly and Company reported results of new data from Phase 3 COV-BARRIER sub-study that indicates baricitinib lowered mortality risk in Covid-19 patients receiving mechanical ventilation or extracorporeal membrane oxygenation (ECMO). Results showed that COVID-19 patients on ECMO who received baricitinib plus standard of care were 46 percent less likely to die by Day 28 compared to patients who received placebo plus standard of care. In the baricitinib group, the cumulative proportion of subjects who died by day 28 was 39.2% as against 58% in the placebo group. Furthermore, by day 60, the cumulative proportion of mortality was 45.1% in participants on baricitinib versus 62% in those on placebo. These findings are based on the COV-BARRIER trial's additional cohort comprising 101 adult subjects. Clinical trial registration # : NCT04421027

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 7th to 13th August 2021.

Country	PHSM Trend	PHSM Change
Tier 4 (High Alert): Daily case incidence per 1M people/day ≥ 80 and/or positivity rate ≥ 12%		
Libya	↓	The three-day lockdown in **Libya** expired, but authorities have imposed a nightly curfew from 18:00-06:00 in its place to combat COVID-19 transmission. The border with Tunisia has also been closed for a week to rising cases.
Morocco	→	Authorities in **Morocco** extended the state of health emergency until 10 September, but have lifted some restrictions for fully-vaccinated individuals, including the nightly curfew and ban on interstate travel.
Namibia	↓	**Namibia** relaxed some COVID-19 measures, including increasing the capacity limits on public gatherings from 50 to 100 people, reopening of some businesses including nightclubs and gyms (with restrictions), and resumption of contact sports with no spectators. Other measures, including a nightly curfew, remain in place until 14 September.
Zimbabwe	→	Level four lockdown measures were extended in **Zimbabwe** amid a continuing rise in COVID-19 transmission. Measures include school closures, a nationwide nightly curfew, and a ban on nonessential intercity travel. The government also announced that vaccinated people could return to religious services.
Tier 3 (Moderate Alert): Daily case incidence per 1M people/day is 20 to <80 and/or positivity rate is 5% to <12%		
Angola	↓	Casinos and gaming rooms are allowed to reopen in **Angola** with some restrictions on capacity and hours of operation.
Rwanda	↓	Authorities in **Rwanda** have eased some COVID-19 restrictions. The nationwide curfew was reduced by 2 hours, on-premise dining is allowed at restaurants and cafes, gyms reopened, capacity limits on public transportation were increased to 75%, and marriage ceremonies are allowed to occur with 50 people in attendance.
Tier 2 (Low Alert): Daily case incidence per 1M people/day is 5 to <20 and/or positivity rate is 3% to 5%		
Cote d'Ivoire	→	The state of health emergency in **Cote d'Ivoire** has been extended until at least 30 September. No new measures have been introduced, but restrictions on international travellers and enforcement of individual protective measures in public spaces (wearing a facemask, social distancing) have been maintained.
Guinea	↑	**Guinea** tightened some COVID-19 measures amid rising cases. Bars and entertainment venues have been closed, a nightly curfew was expanded to the entire nation, and civil servants are now required to present a health pass to access their offices.

Guinea-Bissau	→	Authorities in **Guinea-Bissau** have declared a state of calamity amid rising COVID-19 cases until at least 8 September. No new measures have been imposed, but a mask mandate is maintained for all people in public spaces.
Tier 1 (Standard Precautions): Daily case incidence per 1M people/day is <5 and/or positivity rate is <3%		
Congo	→	**Congo** extended the nationwide state of health security until at least 4 September. Ongoing measures include restrictions on public gatherings to just 3 people, a nightly curfew in the hotspot areas of Brazzaville and Pointe-Noire, and closure of nightclubs.
Madagascar	→	Officials in **Madagascar** are extending the COVID-related state of health emergency until 23 August, but have lifted some other restrictions, including the nightly curfew, and have allowed some businesses to reopen, including nightclubs. A ban on gatherings of 400 people or more remains in effect.

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

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