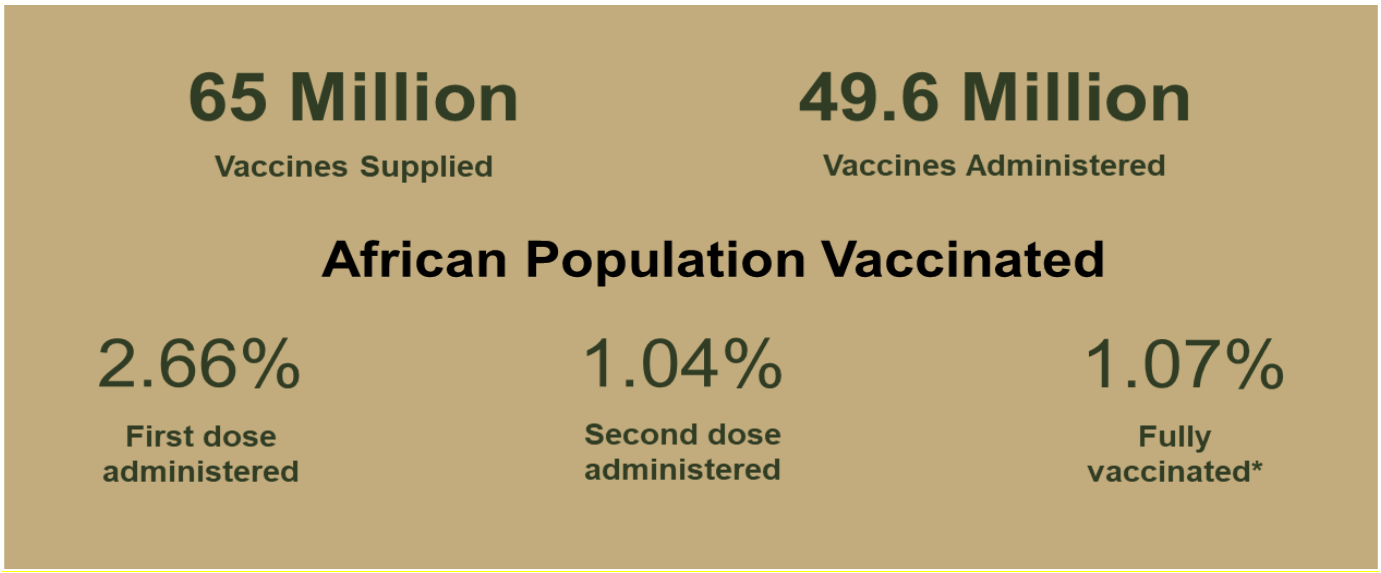
COVID-19 Scientific and Public Health Policy Update[1] – (06 July 2021)

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

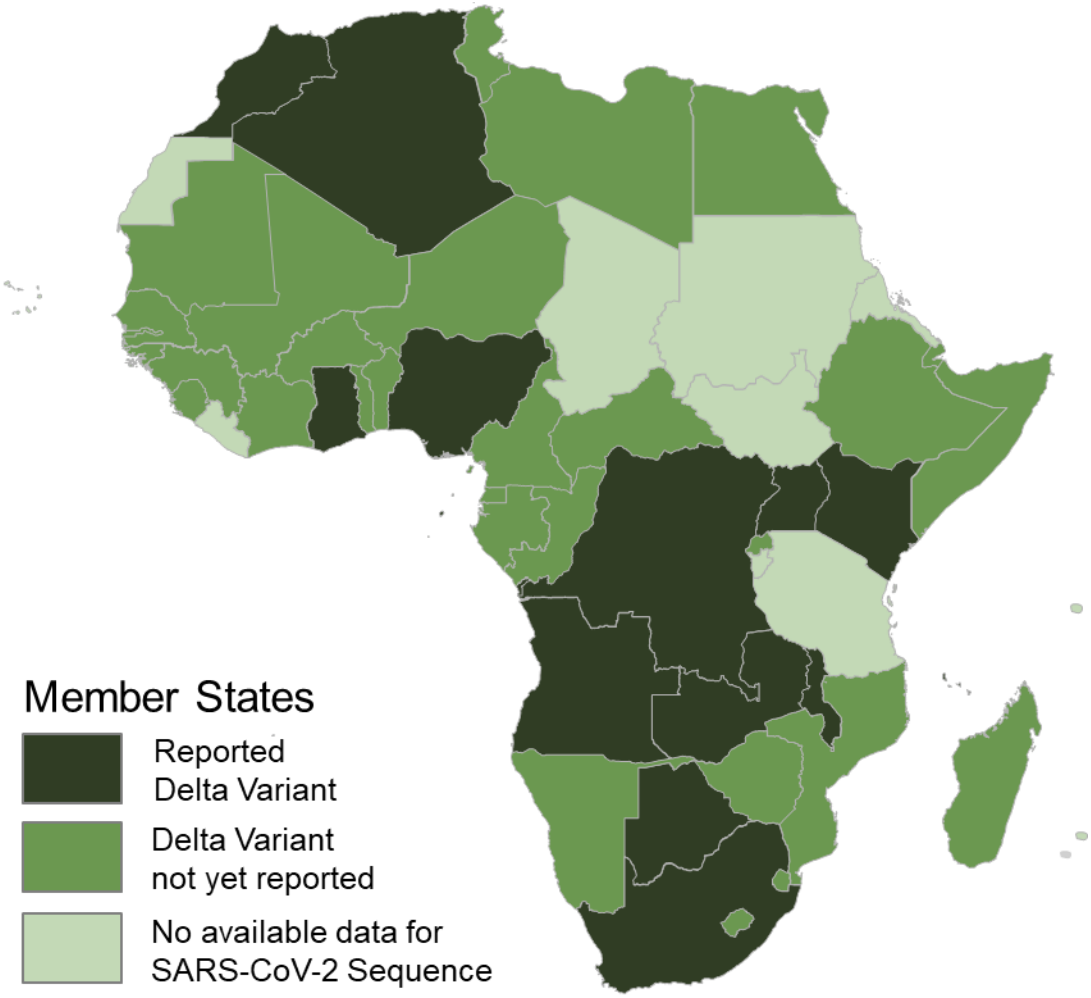


*Received two doses/ one dose of Johnson & Johnson vaccine
https://africacdc.org/covid-19-vaccination/
Updated 30th June 2021

Variants of Concern

- The B.1.617.2 (Delta variant), first reported in India, has spread to more than 96 countries worldwide; 13 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 1st July 2021

Adverse Events Following Immunization (AEFIs)

- **Anaphylaxis after COVID-19 vaccination is rare:** reports show that anaphylaxis has occurred in approximately 2 to 5 people per million vaccinated in the United States. Severe allergic reactions, including anaphylaxis, can occur after any vaccination.
- **Thrombosis with thrombocytopenia syndrome (TTS) after Johnson & Johnson's Janssen (J&J/Janssen) COVID-19 vaccination is rare:** as of 28th June 2021**,** CDC and FDA identified 38 confirmed reports of 12.3 million people who got the J&J/Janssen COVID-19 Vaccine and later developed TTS.
- **Myocarditis and pericarditis after COVID-19 vaccination are rare:** As of 28th June 2021, CDC and FDA have confirmed a total of 518 myocarditis or pericarditis reports among people ages 30 and younger who received mRNA COVID-19 vaccination (Pfizer-BioNTech or Moderna). However, investigations are ongoing to assess whether these reports have any relationship to COVID-19 vaccination.
- **Reports of death after COVID-19 vaccination are rare:** Of more than 324 million doses of COVID-19 vaccines administered in the United States, 5,718 reports of death (0.0018%) have been received. However, it is unclear whether vaccination was the cause.

For further detailed information, click the link here.

B. New guidelines and resources

Since 19th June 2021,

- Africa CDC has published new guidance and resources on:
  - Statement on Covishield and the European Union (EU) Digital COVID Certificate "Green Pass"
- US CDC has published new guidance and resources on:
  - Public Health Guidance for potential COVID-19 exposure associated with travel
  - Expanding COVID-19 vaccine distribution to primary care providers to address disparities in immunization: Guide for Jurisdictions
  - Evaluating SARS-CoV-2 vaccine effectiveness among health care personnel during early phase vaccination
  - Interim Guidance for use of pooling procedures in SARS-CoV-2 diagnostic and screening testing
  - Operational considerations for adapting a contact tracing program to respond to the COVID-19 pandemic in non-US Settings
  - Guidance for reporting SARS-CoV-2 sequencing results
  - Care for breastfeeding people
- WHO has published new guidance and resources on:
  - Technical considerations for implementing a risk-based approach to international travel in the context of COVID-19
  - Policy considerations for implementing a risk-based approach to international travel in the context of COVID-19
  - Ethical Framework for WHO's work in the ACT-Accelerator
  - Protocol template to be used as template for observational study protocols for sentinel surveillance of adverse events of special interest (AESIs) after vaccination with COVID-19 vaccines
  - Implementation guidance for assessments of frontline service readiness: strengthening real-time monitoring of health services in the context of the COVID-19 pandemic
  - Indicator framework for the evaluation of the public health effectiveness of digital proximity tracing solutions
  - Managing family risk: A facilitator's toolbox for empowering families to manage risks during COVID-19
  - A family toolbox for managing health and happiness during COVID-19
  - Recommendations for national SARS-CoV-2 testing strategies and diagnostic capacities
  - Considerations for quarantine of contacts of COVID-19 cases

- FDA has issued press releases on:
  - FDA authorized the use (EUA) for the Janssen COVID-19 vaccine, of an additional batch of vaccine drug substance manufactured at the Emergent facility.
  - FDA Revokes Emergency Use Authorizations for Certain Respirators and Decontamination Systems as Access to N95s Increases Nationwide
  - FDA announced revisions to the patient and provider fact sheets for the Moderna and Pfizer-BioNTech COVID-19 vaccines regarding the suggested increased risks of myocarditis and pericarditis following vaccination.
  - FDA issued a supplement to the 2015 safety communication on reprocessed flexible bronchoscopes

  - FDA issued an emergency use authorization (EUA) for the drug Actemra (tocilizumab) for the treatment of hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen
  - FDA issued a Drug Safety Communication for hand sanitizers, warns that vapors from alcohol-based hand sanitizers can have side effects
  - As of 2nd July, 393 tests and sample collection devices are authorized by the FDA under emergency use authorizations (EUAs).
- ECDC has issued new resources on:
  - Countering online vaccine misinformation in the EU/EEA
  - Indicator framework to evaluate the public health effectiveness of digital proximity tracing solutions
  - Threat Assessment Brief: Implications for the EU/EEA on the spread of the SARS-CoV-2 Delta (B.1.617.2) variant of concern

- PHE has issued new guidance and press releases on:
  - Guidance for arranging or attending a funeral or commemorative event during the coronavirus (COVID-19) pandemic
  - JCVI issues Interim advice on COVID-19 booster vaccination
  - Investigation of SARS-CoV-2 variants of concern: variant risk assessments
  - Guidance for contacts of people with confirmed coronavirus (COVID-19) infection who do not live with the person
  - COVID-19 surge testing outcomes reports: management information
  - COVID-19 Health Inequalities Monitoring in England Tool (CHIME)
  - Stay at home: guidance for households with possible or confirmed coronavirus (COVID-19) infection
  - Guidance for households with grandparents, parents and children living together where someone is at increased risk or has possible or confirmed coronavirus (COVID-19) infection
  - Coronavirus (COVID-19): admission and care of people in care homes
  - COVID-19: guidance on shielding and protecting people defined on medical grounds as extremely vulnerable

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 aimed to measure cross-reactive $CD8^+$ T cell immunity between seasonal coronaviruses that cause the common cold and SARS-CoV-2. The authors measured the frequency of antigen-specific T cells in unexposed pre-pandemic donors and COVID-19 patients presenting mild or severe symptoms so as to evaluate the contribution of pre-existing immunity to seasonal coronaviruses in disease resolution. They engineered an improved multimeric αβ T cell staining "spheromer" reagent for direct, ex vivo detection of antigen-specific T cells at single epitope resolution. The authors found that T cells recognizing peptides conserved among coronaviruses were more abundant and tend to have a "memory" phenotype, compared to those unique to SARS-CoV-2. Significantly, $CD8^+$ T cells with the conserved specificities were much more abundant in COVID-19 patients with mild disease versus those with a more severe illness, suggesting a protective role.
- This observational study among 41 healthy adults who received BNT162b2 aimed to assess whether the vaccine induced antigen specific plasmablasts (PBs) and persistent germinal center (GC) reactions

that are critical for generating high affinity and durable antibody responses. The authors found that the vaccine induced a strong IgG-dominated PB response in blood that peaked one week after the booster immunization. They detected robust SARS-CoV-2 S-binding GC B cell and PB responses after lymph node aspirates in all (14) participants. The responses were detectable after the first immunization but greatly expanded after the booster injection. S-binding GC B cells and PBs persisted for at least 15 weeks after the first immunization (12 weeks after secondary immunization) in 8 of the 10 participants sampled at that time point. The responses to mRNA vaccination were superior to those seen after seasonal influenza virus vaccination in humans.

- This cohort study aimed to assess the early and late antibody kinetics, and the association between antibody levels, clinical symptoms, and disease phase in asymptomatic or mildly symptomatic confirmed SARS-CoV-2 patients. A total of 1334 serum samples were collected from 135 patients and analyzed using three assays for IgG-N (Nucleocapsid), IgG-S (Spike) and IgM antibodies. Of the study participants, 97% were seropositive during the study, and two distinct clusters were identified. These clusters were significantly different in their inflammatory related symptoms. Peak IgG-S was 40.0 AU/ml for the non-inflammatory cluster and 71.5 AU/ml for the inflammatory cluster (P = 0.006), whereas IgG-N peaks were 4.3 and 5.87 (P = 0.023) respectively. The authors designed a decision tree model to predict the disease phase based on the serological titer levels, and had an overall accuracy of 80.7%. The specific profile of seroconversion and decay of serum antibodies can be used to predict the time-course from the acute infection.
- This study used a series of computational approaches for data integration, network analysis, computer simulation, and machine learning to identify novel SARS-CoV-2–induced pathways that could be targeted therapeutically by repurposing existing and approved drugs. Their analysis identified 200 approved drugs, along with their mechanisms of action (MoAs), that may be effective against COVID-19. Forty (40) of which are already in COVID-19 clinical trials. Using artificial neural network analysis, the authors classified the 200 drugs into nine distinct pathways, within two overarching MoAs: viral replication (126) and immune response (74). Two drugs (proguanil and sulfasalazine) implicated in viral replication were shown to inhibit replication in cell assays. This study opens new avenues for the rapid repurposing of approved drugs into clinical trials.
- This study describes the use of a well tolerated antiandrogen drug, enzalutamide, to reduce transmembrane serine protease 2 (TMPRSS2) levels in human lung cells and in mouse lung. Cellular entry of SARS-CoV-2 requires host proteins expressed on the epithelial cell surface, most essential are TMPRSS2 and angiotensin-converting enzyme 2 (ACE2). In support of their experimental data, analysis of existing datasets shows striking co-expression of androgen receptor and TMPRSS2, including in specific lung cell types targeted by SARS-CoV-2. This study provides evidence to support clinical trials to assess the efficacy of antiandrogens as a treatment option for COVID-19.

Vaccines

- This phase 3, randomised, observer-blinded, placebo-controlled trial among 15,187 adults in the UK aimed to assess the efficacy, immunogenicity, and safety of NVX-CoV2373 (Novavax), a recombinant nanoparticle vaccine. The authors report that a two-dose regimen of the NVX-CoV2373 vaccine conferred 89.7% protection against SARS-CoV-2 infection and showed high efficacy against the B.1.1.7 variant. NVX-CoV2373 can be stored at standard refrigeration temperatures and has the potential to induce a broad epitope response to the spike protein antigen.
- This phase 2, open label, randomised, controlled trial among adults in Spain aimed to assess the immunogenicity and reactogenicity of BNT162b2 administered as second dose in 676 participants primed with ChAdOx1-S. The authors report that in the intervention group, geometric mean titres of receptor binding domain (RBD) antibodies increased from 71.46 BAU/mL at baseline to 7756.68 BAU/mL at day 14 (p<0·0001). IgG against trimeric spike protein increased from 98.40 BAU/mL to 3684.87 BAU/mL. The interventional:control ratio was 77.69 for RBD protein and 36.4 for trimeric spike protein IgG. Reactions were mild (68%) or moderate (30%), with injection site pain (88%), induration (35%), headache (44%), and myalgia (43%) the most commonly reported adverse events. There were no serious adverse events reported.

- This phase 1/2, double-blind, randomised, controlled clinical trial aimed to assess the safety, tolerability, and immunogenicity of a candidate COVID-19 vaccine, CoronaVac, containing inactivated SARS-CoV-2, in children and adolescents aged 3–17 years. A total of 550 participants received at least one dose of vaccine or aluminium hydroxide only (n=71 for phase 1 and n=479 for phase 2; safety population). The authors report that most adverse reactions were mild and moderate in severity. Injection site pain was the most frequently reported event (13%). In phase 1, 100% seroconversion was observed in both 1.5 µg and 3.0 µg groups, with the geometric mean titres of 55.0 and 117.4. In phase 2, seroconversion was seen in 96.8% in the 1·5 µg group and 100% in the 3.0 µg group, with the geometric mean titres of 86.4 and 142.2. Their results support the use of 3.0 µg dose with a two-immunisation schedule for further studies in children and adolescents.
- This study assessed the effect of antibody responses from 20 human sera obtained 2 or 4 weeks after 2nd dose of BNT162b2 (Pfizer/BioNTech) to SARS-CoV-2 wild-type virus and spike protein variants B.1.617.1, B.1.617.2, B.1.618 (all first identified in India) and B.1.525 (first identified in Nigeria). The authors found that all sera samples neutralized the SARS-CoV-2 wild-type (WA1/2020) virus and variant viruses B.1.525, B.1.617.1, B.1.617.2, and B.1.618. Neutralization of all variants, except B.1.617.1, was only modestly reduced relative to the wild-type virus. They recommend to increase the proportion of the population immunized with current safe and effective authorized vaccines to minimize the emergence of new variants and end the COVID-19 pandemic.
- This multinational network cohort study aimed to quantify the background incidence rates of 15 prespecified adverse events of special interest (AESIs) associated with covid-19 vaccines. The study involved 126,661,070 people enrolled between 1st January 2017 and 31st December 2019 from 13 databases from eight countries: Australia, France, Germany, Japan, the Netherlands, Spain, the United Kingdom, and the United States. The authors found that background incidence rates varied greatly across databases, similar age and sex trends were observed for each AESI. Rates of deep vein thrombosis, acute myocardial infarction, hemorrhagic and non-hemorrhagic stroke, pulmonary embolism, Bell's palsy, immune thrombocytopenia, Guillain-Barré syndrome, and disseminated intravascular coagulation increased with age.
- This cohort analysis aimed to describe the demographic profile of COVID-19 patients, investigate the risk of hospital admission for COVID-19, and estimate effectiveness of BNT1682b and ChAdOx1 in preventing COVID-19 hospital admissions in *S* gene-positive cases in Scotland. The authors report that by May 2021, the Delta variant became the dominant SARS-CoV-2 strain in Scotland. B.1.617.2 made up 97% of S-gene positive cases, which comprises 40% (7,723/19,543) of all cases and 36% (134/377) of hospitalizations. S-gene positive cases were associated with increased hospitalization risk (aHR 1.85, 95% CI 1.39-2.47) compared to S-gene negative cases. Both BNT1682b and ChAdOx1 vaccines were effective in preventing hospitalization regardless of S-gene status.
- This nested incident-matched case-control study and a confirmatory self-controlled case series analysis aimed to estimate the associations between exposure to first-dose ChAdOx1 or BNT162b2 vaccination and hematological and vascular adverse events. The authors report that within 0-27 days after the 1st dose, ChAdOx1 vaccination was associated with rare but higher occurrences of Idiopathic thrombocytopenic purpura (aRR 5.77, 95% CI 2.41-13.83) representing 1.13 (95% CI 0.62-1.63) incident cases per 100,000 doses, arterial thromboembolic events (aRR 1.22, 95% CI 1.12-1.34), Hemorrhagic events (aRR 1.48, 95% CI 1.12-1.96). No positive associations were seen between BNT162b2 and thrombocytopenic, thromboembolic, or hemorrhagic events.
- This clinical trial among health care workers in Germany aimed to assess the anti-SARS-CoV-2 antibody ratio after different immune stimulations (natural infection or vaccination). The authors compared the presence of anti-SARS-CoV-2 immunglobulin G (IgG) antibody ratio after natural infection, or vaccination with one or two doses of BNT162b2, or one dose of ChAdOx1 (Vaxzevria) vaccine. They found that 2 doses of BNT162b2 elicited significantly higher antibody levels compared to a single dose of either BNT162b2 or ChAdOx1 vaccines or Immunity obtained from previous PCR-confirmed SARS-CoV-2 infection. [*not peer reviewed*]
- This case series aimed to describe antibody responses and vaccine reactions in 30 recipients of solid organ transplants who had a suboptimal response to 2 doses of either BNT162b2 or mRNA-1273 and

subsequently received a third dose of either Ad26.COV2.S, BNT162b2, or mRNA-1273. The authors performed antibody testing at a median of 9 days before and at a median of 14 days after receiveing the 3rd dose. They report that after the 3rd dose, all 6 patients with low-positive antibody titers before the 3rd dose had high-positive antibody titers and of 24 patients with negative titers before the 3rd dose, 6 had high-positive antibody titers, 2 had low-positive antibody titres, and 16 remained negative. Fifteen patients reported mild or moderate local reactions, and 1 reported severe arm pain. The most frequent systemic reaction was mild or moderate fatigue in 14 participants; 1 patient reported severe headache, and 1 patient reported severe myalgia.

- This prospective observational study aimed to investigate the safety and effectiveness of the BNT162b2 and ChAdOx1 vaccines in a UK community setting. The authors examined the proportion and probability of self reported systemic and local side-effects within 8 days of vaccination in individuals using the COVID Symptom Study app. There were 627,383 individuals who reported being vaccinated between 8th Dec 2020 and 10th March 2021. Systemic side-effects were reported by 13.5% of individuals after the first dose of BNT162b2, by 22.0% after the second dose of BNT162b2, and by 33.7% after the first dose of ChAdOx1. Local side-effects were reported by 71.9% of individuals after the first dose of BNT162b2, by 68.5% after the second dose of BNT162b2, and by 58.7% after the first dose of ChAdOx1. Systemic and local side-effects were more common among individuals with previous SARS-CoV-2 infection than among those without known past infection.
- This study describes the generation and preclinical assessment of a ChAdOx1-vectored vaccine against the variant of concern B.1.351 (AZD2816). The authors demonstrate that AZD2816 is immunogenic after a single dose and when used as a booster dose in animals primed with original vaccine AZD1222, they saw no evidence of original antigenic sin but high titre antibodies against a number of variant spike proteins. Neutralisation titres against B.1.351 (Beta), B.1.617.1 (Kappa) and B.1.617.2 (Delta), were induced in the boost regimens. Their data support the ongoing clinical development and testing of the new variant vaccine.[*not peer reviewed*]
- This prospective cohort study among 3975 health care workers aimed to assess the effectiveness of mRNA (BNT162b2 and mRNA-1273) vaccines in prevention and attenuation of Covid-19. The authors report that SARS-CoV-2 was detected in 204 participants (5%), of whom 5 were fully vaccinated (≥14 days after dose 2), 11 partially vaccinated (≥14 days after dose 1 and <14 days after dose 2), and 156 unvaccinated;32 participants with indeterminate vaccination status (<14 days after dose 1) were excluded.The adjusted vaccine effectiveness was 91% (95 CI, 76-97) with full vaccination and 81% (95 CI, 64 to 90) with partial vaccination. Among participants with SARS-CoV-2 infection, the mean viral RNA load was 40% lower (95 CI, 16 to 57) in partially or fully vaccinated participants than in unvaccinated participants. In addition, the risk of febrile symptoms was 58% lower (relative risk, 0.42; 95 CI, 0.18 to 0.98) and the duration of illness was shorter, with 2.3 fewer days spent sick in bed (95 CI, 0.8 to 3.7).
- This study aimed to assess the ease of reading (i.e., readability) of the EUA-approved fact sheets for the vaccines currently available in the United States (Pfizer, Moderna and Janssen), the V-Safe adverse event survey script, and the Centers for Disease Control and Prevention (CDC) website on COVID-19 vaccines. Only the V-Safe adverse event survey script met readability standards for adequate comprehension. The authors recommend that simplified information materials should be developed to ensure that the public fully understands information regarding COVID-19 vaccines, [*not peer reviewed*]
- This phase 3, randomised, double blinded, multicentre clinical trial among 25798 adults in 25 indian hospitals aimed to evaluate the efficacy, safety, and immunological lot consistency of BBV152, a whole virion inactivated SARS CoV 2 vaccine. BBV152 was found to be immunogenic and highly efficacious against symptomatic and asymptomatic COVID 19 variant associated disease, particularly against severe disease in adults. Vaccination was well tolerated with an overall incidence of adverse events observed over a median of 146 days that was lower than that observed with other COVID-19 vaccines. [*not peer reviewed*]

Diagnostics

- This study reports on a microfluidic point-of-care (POC) test that can profile the antibody response against multiple SARS-CoV-2 antigens; spike S1 (S1), nucleocapsid (N), and the receptor binding domain (RBD), simultaneously from 60 µl of blood, plasma, or serum. The authors assessed the levels of antibodies in plasma samples from 31 individuals (with longitudinal sampling) with severe COVID-19, 41 healthy individuals, and 18 individuals with seasonal coronavirus infections. They report that their POC assay achieved high sensitivity and specificity, tracked seroconversion, and showed good concordance with a live virus microneutralization assay. They can also detect a prognostic biomarker of severity, IP-10 (interferon-γ–induced protein 10), on the same chip. The test can be deployed globally as it requires minimal user intervention and is read by a handeheld detector.
- This study describes an immunoaffinity purification approach followed by a high-resolution mass spectrometry-based targeted qualitative assay capable of detecting SARS-CoV-2 viral antigen from nasopharyngeal swab samples. The authors targeted the nucleocapsid protein. Using the optimized target assay, they analyzed 88 positive and 88 negative nasopharyngeal swab samples for validation. They observed a 98% (95% CI = 0.922–0.997) (86/88) sensitivity and 100% (95% CI = 0.958–1.000) (88/88) specificity using RT-PCR-based molecular testing as the reference method. Their results demonstrate that direct detection of infectious agents from clinical samples by tandem mass spectrometry-based assays have potential to be deployed as diagnostic assays in clinical laboratories; which has until now been limited to analysis of pure microbial cultures.
- This cross-sectional study among 2542 asymptomatic adults in a community with a SARS-CoV-2 incidence of 1.93% aimed to validate Roche SARS-CoV-2 Rapid Antigen Test as a screening tool using RT-PCR test as the reference standard. The test showed a sensitivity of 71.43% (CI 95%: 56.74 – 83.42) and a specificity of 99.68% (CI 95%: 99.37 – 99.86). Positive Predictive Value was 81.4 (CI 95% 66.6 – 91.61) and Negative Predictive Value was 99.44 (CI 95% 99.06 – 99.69). Test sensitivity was related to viral load, with higher sensitivity in RT-PCR cycle threshold (Ct) values under 25 (93.75%, CI 95%: 71.96 – 98.93), that dropped to 29.41% (CI 95%: 10.31- 55.96) in RT-PCR Ct values above 25. This study suggests that rapid antigen tests are less effective in asymptomatic population, when compared with RT-PCR.
- In this study, the authors developed a high-precision, cost-efficient SARS-CoV-2 whole-genome sequencing platform for COVID-19 genomic surveillance, CorvGenSurv (Coronavirus Genomic Surveillance). CorvGenSurv directly amplified viral RNA from COVID-19 patients' Nasopharyngeal/ Oropharyngeal swab specimens and sequenced the SARS-CoV-2 whole genome in three segments by long-read, high-throughput sequencing. Sequencing of the whole genome in three segments significantly reduced sequencing data waste, thereby preventing dropouts in genome coverage. They identified new amino acid mutations in the NSP3, NSP4, RdRP (NSP12), ORF8, and N proteins. Mutations in these proteins have the potential to trigger immune escape, alter viral replication capacity, or modulate viral immune suppression.
- This study reports on a next-generation sequencing of pooled samples tagged with sample-specific molecular barcodes. The authors named the assay SwabSeq. It enables the testing of thousands of nasal or saliva samples for SARS-CoV-2 RNA in a single run without the need for RNA extraction. They used SwabSeq to perform 80,000 tests, with an analytical sensitivity and specificity comparable to or better than traditional qPCR tests, in less than two months with turnaround times of less than 24 hours. Their assay offers a potential solution to the need for population-wide testing.

Care and Treatment

- This systematic review and meta analysis aimed to evaluate the effect of sofosbuvir/daclatasvir (SOF/DCV) on mortality, the need for ICU admission or invasive mechanical ventilation (IMV) and clinical recovery in patients with COVID-19. Four studies with a total of 231 patients were included. Three studies were randomised controlled trial, and one study was non-randomised. The intervention group was SOF/DCV, defined as 400 mg SOF and 60 mg DCV to treat COVID-19. The control group was the standard of care or placebo set by each trial/studies. The authors report that SOF/DCV was associated with lower mortality (RR: 0.31 (0.12, 0.78); p=0.013; I^2: 0%) and reduced need for ICU admission or IMV (RR: 0.35 (0.18, 0.69); p=0.002; I^2: 0%). Clinical recovery was achieved more frequently in the SOF/DCV group (RR: 1.20 (1.04, 1.37); p=0.011; I^2: 21.1%).
- This retrospective case series aimed to describe myocarditis presenting after COVID-19 vaccination (messenger RNA) within the Military Health System. The authors included a total of 23 male patients (22 currently serving, 1 retiree; median [range] age, 25 [20-51] years) who received the vaccine between 1st January and 30th April 2021. They report that myocarditis was identified within 4 days of receipt of a COVID-19 vaccine. For most patients (n = 20), the diagnosis was made after the second dose of mRNA COVID-19 vaccine.
- This cohort study among 97 covid-19 patients with anosmia (acute smell loss beyond 7 days) was aimed to clarify their clinical course and prognosis after 1 year. The authors performed repeated olfactory function evaluations, The authors report that out of the 97 pateints, 51 (52.6%) underwent both subjective and objective olfactory test, and 46 (47.4%) underwent subjective assessment alone After subjective assessment at 4 months, 23 of 51 patients (45.1%) reported full recovery of olfaction, 27 of 51 patients (52.9%) reported partial recovery, and 1 of 51 patients (2.0%) reported no recovery. On psychophysical testing, 43 of 51 patients (84.3%) were objectively normosmic, including 19 of 27 (70.0%) who self-evaluated as only partially recovered. Persistent COVID-19–related anosmia has an excellent prognosis with nearly complete recovery at 1 year.
- This qualitative study aimed to better understand the experiences of bereaved family members of patients who died in an ICU during the COVID-19 pandemic, from the time of hospital admission until after the patient's death. The participants reported difficulties in establishing a bond with the ICU team and maintaining a relationship with their loved ones during their stay in the ICU. They also described a feeling of "stolen moments" after the death of their loved one, generating strong feelings of disbelief that could potentially lead to complicated grieving. Specific family-centered crisis guidelines are needed to improve experiences for patients, families, and clinicians experiences.
- This retrospective study among 343 COVID-19 patients admitted to Kingston Hospital in the UK aimed to investigate the correlation between abnormal liver function and adverse outcomes. The authors excluded those with a history of liver disease, 299 patients had liver function tests performed with abnormalities demonstrated in 44.8% of individuals. Derangement of liver function was associated with greater need for ventilatory support (p<0.001), admission to high dependency unit or intensive care (p<0.001) and increased length of hospital stay (p<0.001). Liver dysfunction was more common in those of non-white ethnicity (p=0.007) and correlated with higher levels of C reactive protein (p=0.01) and ferritin (p<0.001).
- These cohort studies aimed to assess the association between routinely prescribed non-steroidal anti-inflammatory drugs (NSAIDs) and deaths from COVID-19. In study 1, they included 536,423 current NSAID users and 1,927,284 non-users in the general population. They observed no evidence of difference in risk of COVID-19 related death associated with current use (HR 0.96, 95% CI 0.80 to 1.14) in the multivariable-adjusted model. In study 2, they included 1,708,781 people with rheumatoid arthritis/osteoarthritis, of whom 175,495 (10%) were current NSAID users. In the multivariable-adjusted model, they observed a lower risk of COVID-19 related death (HR 0.78, 95% CI 0.64 to 0.94) associated with current use of NSAID versus non-use. The authors found no evidence of a harmful effect of routinely prescribed NSAIDs on COVID-19 related deaths.
- This multicentre nationwide cohort study among 8392 admitted patients in Spain aimed to determine the proportion of patients with COVID-19 who were readmitted to the hospital and the most common causes and the factors associated with readmission. The authors report that 298 patients (4.2%) out

of 7137 patients were readmitted after being discharged. 1541 (17.7%) died during the index admission and 35 died during hospital readmission (11.7%, p = 0.007). The median time from discharge to readmission was 7 days (IQR 3–15 days). The most frequent causes of hospital readmission were worsening of previous pneumonia (54%), bacterial infection (13%), venous thromboembolism (5%), and heart failure (5%). Advanced age and comorbidity were associated with increased risk of readmission.

Epidemiology

- This retrospective observational study of 2826 patients with COVID-19-associated rhino-orbital-cerebral mucormycosis (ROCM) in India aimed to determine the patient demographics, risk factors including comorbidities, and medications used to treat COVID-19, presenting symptoms and signs, and the outcome of management. The authors conclude that corticosteroids and diabetes mellitus are the most important predisposing factors in the development of COVID-19-associated ROCM. COVID-19 patients must be followed up beyond recovery. Awareness of red flag symptoms and signs, high index of clinical suspicion, prompt diagnosis, and early initiation of treatment with amphotericin B, aggressive surgical debridement of the paranasal sinus, and orbital exenteration, where indicated, are essential for successful outcome.
- This observational study aimed to examine the dynamics of SARS-CoV-2 seroprevalence among 9922 adult Kenyan blood donors throughout the course of the first epidemic wave (from 30th April to 30th September 2020). The authors report that crude seroprevalence was 9.4% (95% CI, 8.8–9.9%) with little variation by age or sex. There was marked variation in seroprevalence over time and place with a generally increasing trend over time. Nairobi, Mombasa and the Coastal Region outside Mombasa were found to have a steep rise in seroprevalance across the study period. Although most people remained susceptible, SARS-CoV-2 had spread widely in Kenya with apparently low associated mortality.
- This study used an agent based model with SEIR disease dynamics to simulate SARS-CoV-2 spread over 90 days in a population of 5000 university students. The study aimed to assess whether quarantine was still a useful method for preventing transmission and whether an increased surveillance testing protocol was as effective as quarantine at limiting viral transmission in an environmnet where 100% of the student population is vaccinated. The authors also considered that vaccine effectiveness may be impacted by vaccine type, variants, and/or waning immunity. The authors report that weekly surveillance testing at 90% vaccine effectiveness only marginally reduces viral transmission as compared to no testing. However, at 50%–75% vaccine effectiveness, surveillance testing can provide over 10-fold reduction in the number of infections. They also show that a 10 day quaratine protocol for exposures has limited effect on infections until vaccine effectiveness drops to 50%, and that increased surveillance testing for exposures is atleast as effective as quarantine at limiting infections. [*not peer reviewed*]
- This analysis of vaccine breakthrough infections in a cohort of over 100 health care workers across 3 centers in India revealed that they were predominantly due to B.1.617.2 (Delta) (98/133). Compared to wild-type (WT Wuhan-1), B.1.617.2 showed an approximate 8-fold reduction in vaccine-elicited antibody production. Serum neutralizing titers were lower in participants vaccinated with ChAdOx-1 compared to BNT162b2 (geometric mean titre 654 vs. 3372, p = .0006). Their combined epidemiological and in vitro data indicate that the dominance of the Delta variant in India has been most likely driven by a combination of evasion of neutralising antibodies in previously infected individuals and increased virus infectivity. Breakthrough transmission clusters in hospitals associated with the Delta variant are concerning and indicate that infection control measures need continue in the post-vaccination era.[*not peer reviewed*]
- This study compared antibiotic prescription practices using data from the Wisconsin Health System during the pre-COVID-19 period and the COVID-19 period. The authors report that ambulatory encounters were similar during both periods (637 000 vs 661 000 per month; P = .24). Antibiotic prescribing rates increased during winter respiratory viral seasons during the pre-pandemic period. In contrast, antibiotic prescribing rates decreased in the short term and remained low throughout the

pandemic period. Adjusting for seasonality, monthly antibiotic prescriptions for RTI fell 79% from 10.5 to 2.2 prescriptions per 1000 patient encounters (P < .001). Their results suggest that COVID-19 transmission mitigation strategies may help curb respiratory viral diseases beyond SARS-CoV-2 and, indirectly, decrease inappropriate antibiotic prescribing.

- This multifaceted intervention case series aimed to analyze how Boston University (BU) fully reopened its campus in the fall of 2020 and controlled COVID-19 transmission despite worsening transmission in Boston, Massachusetts. Between August and December 2020, BU conducted more than 500 000 COVID-19 tests and identified 719 individuals with COVID-19, including 496 students (69.0%), 11 faculty (1.5%), and 212 staff (29.5%). Overall, 718 individuals, or 1.8% of the BU community, had test results positive for SARS-CoV-2. Of 837 close contacts traced, 86 individuals (10.3%) had test results positive for COVID-19. BU contact tracers identified a source of transmission for 370 individuals (51.5%), with 206 individuals (55.7%) identifying a non-BU source. Most transmission occurred off campus, and there was no evidence of classroom transmission.
- This modelling study aimed to identify the secondary transmission pattern and risk factors for infection with SARS-CoV-2 in Rwanda. The authors used the contact tracing data in Rwanda for understanding the geographic patterns of COVID-19 to inform targeted interventions.The results showed that COVID-19 cases are localised mainly in the central regions and in the southwest of Rwanda, there were some clusters in the northeast. Relationship to the index case, being male and coworkers were the important risk factors identified for COVID-19 transmission in Rwanda.

Infection Prevention and Control

- This study describes the ability of bidimensional nanoparticles, Graphene (G) and Graphene oxide (GO), to interact with microorganisms and provide an opportunity to develop engineered textiles for use in PPE such as masks. GO inhibit SARS-CoV-2 infection of VERO cells. When G/GO functionalized polyurethane or cotton were in contact SARS-CoV-2, the infectivity of the fabric was nearly completely inhibited. Their findings constitute an innovative nanomaterial-based strategy to significantly increase PPE efficacy.
- This study analyzes the acceptable methods for respirator decontamination and reuse, and scores them according to a number of variables that the authors have defined as being crucial (including cost, risk, complexity, time, etc.) to help healthcare facilities decide which method of decontamination is right for them incase of an emergency situation where they need to reuse respirators.

Non-pharmaceutical interventions, social distancing

- This nationwide cross-sectional study among 2.9 million US households aimed to assess the association between social gatherings and SARS-CoV-2 transmission by studying whether COVID-19 rates increase after birthdays in a household. The authors found that, among households in the top decile of county COVID-19 prevalence, those with birthdays had 8.6 more diagnoses per 10 000 individuals compared with households without a birthday, a relative increase of 31% of county-level prevalence, an increase in COVID-19 diagnoses of 15.8 per 10 000 persons after a child birthday, and an increase in COVID-19 diagnoses of 5.8 per 10 000 among households with an adult birthday. This study suggests that events that lead to small and informal social gatherings, such as birthdays, and in particular, children's birthdays, are a potentially important source in SARS-CoV-2 transmission.
- This study assessed the effects of fluctuating control measures on the evolution and epidemiology of SARS-CoV-2 lineages under the elimination strategy in Hong Kong. The authors analysed more than 1700 genome sequences (17% of confirmed cases) from 23rd January 2020 to 26th January 2021. The authors report that only three introductions were responsible for 90% of locally-acquired cases, two of which circulated cryptically for weeks while less stringent measures were in place. Their results also show that contact tracing was efficient, but averting outbreaks from new introductions requires heightened border control and enhanced community surveillance during periods of lower control level stringency. [*not peer reviewed*]

- This case control study examined the association between mask mandates in Kansas counties and COVID-19 cases, hospitalizations, and deaths. The Kansas executive order that took effect on July 3 was adopted by only 15 counties, and 68 counties did not have a mandate through October. By mid-October 2020, counties that adopted the July mask mandate experienced significantly lower rates of COVID-19 cases, hospitalizations, and deaths compared with those that did not. A second mask mandate order took effect on November 25, and 40 additional counties adopted it. Through December 4, cases were lower by 20.33 (95% CI -26.54 to -14.12) per day in mask relative to no mask counties. Similar patterns were seen for hospitalizations and deaths.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 3rd July 2021, Bharat Biotech, a global leader in vaccine development and innovation, announced its safety and efficacy analysis data from a double-blind, randomised, multicentre Phase III clinical trials of COVAXIN, a whole virion inactivated vaccine against SARS-CoV2. Data indicates that COVAXIN was well tolerated with an overall incidence of adverse events observed over a median of 146 days that was lower than that observed with other COVID-19 vaccines. Phase 3 clinical trials of COVAXIN was an event driven analysis of 130 symptomatic COVID-19 cases, reported at least two weeks after the 2nd dose, conducted at 25 sites across India. COVAXIN is formulated with a novel Algel+IMDG adjuvant. IMDG is a TLR7/8 agonist known to induce memory T cell responses along with strong neutralizing antibodies. The activation of cell mediated immune responses is especially valuable in a multi epitope vaccine such as COVAXIN, where immune protection can be achieved from S, RBD and N proteins alike.
- On 1st July 2021, Johnson & Johnson (NYSE: JNJ) (the Company) announced data that demonstrated its single-shot COVID-19 vaccine generated strong, persistent activity against the rapidly spreading Delta variant and other highly prevalent SARS-CoV-2 viral variants. In addition, the data indicated that the durability of the immune response lasted through at least eight months. The two preprint study summaries have been submitted to bioRxiv.
- On 30th June 2021, World Bank Group's International Finance Corporation (IFC)IFC, the French Development institution Proparco, DEG - the German development finance institution, and the U.S. International Development Finance Corporation (DFC) announced a joint financing package for Aspen Pharmacare Holdings Limited, a leading pharmaceutical company in South Africa that is playing a major role producing COVID-19 treatment therapies and vaccines on the African continent. Aspen Pharmacare is set to receive a long-term funding package of nearly $713m (€600m) to boost the production of Covid-19 vaccines for countries in the African continent.
- On 29th June 2021, Moderna, Inc. (NASDAQ: MRNA), a biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines, announced new results from in vitro neutralization studies of sera from individuals vaccinated with the Moderna COVID-19 Vaccine showing activity against variants of SARS-CoV-2. Vaccination with the Moderna COVID-19 Vaccine produced neutralizing titers against all variants tested, including additional versions of the Beta variant (B.1.351, first identified in South Africa), three lineage variants of B.1.617 (first identified in India), including the Kappa (B.1.617.1) and the Delta variants (B.1.617.2); the Eta variant (B.1.525, first identified in Nigeria); and the A.23.1 and A.VOI.V2 variants first identified in Uganda and Angola, respectively. These data are submitted as a preprint to bioRxiv.
- On 29th June 2021, Moderna, Inc. (NASDAQ: MRNA), announced that the government of India has issued a registration certificate and a permission to import the COVID-19 Vaccine Moderna for restricted use in an emergency situation in adults aged 18 years and older. Moderna has also received emergency (or other conditional, interim or provisional) authorization for use of its COVID-19 vaccine from health agencies in more than 50 countries and an Emergency Use Listing (EUL) from the World Health Organization (WHO).

- On 29th June 2021, Altimmune, Inc. (NASDAQ: ALT), a clinical-stage biopharmaceutical company, announced its decision to discontinue the development of its investigational Covid-19 vaccine, AdCOVID, due to lower responses in the Phase I clinical trial. The Phase 1 AdCOVID clinical trial is evaluating the safety and immunogenicity of the intranasally administered vaccine candidate in approximately 80 healthy adult volunteers between the ages of 18 and 55. Subjects received either 1 or 2 doses of AdCOVID as a nasal spray at 3 dose levels. Data showed that the vaccine candidate was well-tolerated with its overall adverse event profile in line with intranasal saline placebo. Immunogenicity data of AdCOVID showed reduced immune responses than anticipated for all the immune parameters analysed. In addition, Altimmune, Inc. decided to terminate further enrolment in Phase I/II clinical trial of its immune-modulating therapeutic, T-COVID, for treating early Covid-19 patients. The company was unable to enrol participants aged 65 years or those at high risk due to existing comorbidities in the third cohort to assess the efficacy of T- COVID. This was due to availability of authorised Covid-19 vaccines in the US which reduced disease incidence thus, lowered the number of patients who met the trial criteria.

Therapeutics trials:

- On 28th June 2021, RedHill Biopharma Ltd. (NASDAQ: RDHL), a specialty biopharmaceutical company, reported preliminary results of a new preclinical study showing potent inhibition of COVID-19 variants of concern by opaganib (Yeliva®, ABC294640). Opaganib, a leading novel investigational oral pill in development for the treatment of COVID-19, is a unique host-targeted, dual antiviral and anti-inflammatory drug that acts on the cause and effect of COVID-19. It exerts its antiviral effect by selectively inhibiting sphingosine kinase-2 (SK2), a key enzyme produced in human cells that can be recruited by the virus to support its replication. According to preliminary data, opaganib demonstrated a potent hindrance of both the Beta (South African) and Gamma (Brazilian) variants at non-cytotoxic doses. The drug yielded positive results in the Phase II clinical trial in the US and is undergoing a global Phase II/III study in 475 hospitalized Covid-19 patients.
- On 25th June 2021, Roche (SIX: RO, ROG; OTCQX: RHHBY) announced that the U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for intravenous Actemra/RoActemra® (tocilizumab) for the treatment of COVID-19 in hospitalized adults and pediatric patients (two years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). The EUA is based on results from four randomized, controlled studies that evaluated Actemra/RoActemra for the treatment of COVID-19 in more than 5,500 hospitalized patients. The results of these studies suggest that Actemra/RoActemra may improve outcomes in patients receiving corticosteroids and requiring supplemental oxygen or breathing support.
- On 23rd June 2021, Tiziana Life Sciences plc (NASDAQ: TLSA, LSE: TILS), a biotechnology company focused on innovative therapeutics for oncology, neurology, inflammation and infectious diseases, announced that it has signed an agreement with FHI Clinical, a global clinical contract research organization (CRO), to conduct a Phase 2 randomized, placebo-controlled, double-blind *Proof-of-concept* study in Brazil to evaluate the safety, tolerability and efficacy of intranasal Foralumab in hospitalized patients with severe coronavirus disease 2019 (COVID-19) and pulmonary inflammation. Patients will be randomized 1:1 to receive intranasal Foralumab 100 µg. Additionally, the study will also evaluate the effect of Foralumab on resolution of symptoms by chest CT, inflammatory biomarkers, T-cell subpopulations, safety and mucosal inflammatory response following 14 days of intranasal administration. Foralumab is a fully human anti-CD3 monoclonal antibody. The nasal and oral doses of the drug showed an ability to stimulate Tregs in animal studies and could be used as immunotherapy for autoimmune as well as inflammatory diseases.
- On 21st June 2021, Tonix Pharmaceuticals Holding Corp. (NASDAQ: TNXP), a clinical-stage biopharmaceutical company, announced its plans to develop TNX-102 SL (cyclobenzaprine HCl sublingual tablets) as a potential treatment for Long COVID Syndrome (Long COVID) which is now known officially as Post-Acute Sequelae of COVID-19 (PASC1). A formulation of cyclobenzaprine hydrochloride, TNX-102 SL offers quick transmucosal absorption and also lowers the production of

norcyclobenzaprine, a long half-life active metabolite. Tonix plans to meet with the U.S. Food and Drug Administration (FDA) in the third quarter of 2021 to seek agreement on the design of a potential Phase 2 pivotal study and the overall clinical development plan to qualify TNX-102 SL as an indicated treatment for Long COVID.

- On 18th June 2021, Edesa Biotech, Inc. (NASDAQ: EDSA), a clinical-stage biopharmaceutical company focused on inflammatory and immune-related diseases, reported that an independent Data and Safety Monitoring Board (DSMB) has completed an interim review of the company's COVID-19 drug candidate (EB05), and based on blinded comparative data, has recommended that the company's international study continue as planned. An investigational monoclonal antibody, EB05, can potentially modulate the overactive and dysfunctional immune response linked with acute respiratory distress syndrome (ARDS), a leading cause of Covid-19 death. The drug hinders toll-like receptor 4 (TLR4) signaling, a key mediator of inflammation that causes acute lung injury activated by SARS-CoV2, SARS-CoV1 and influenza viruses.

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

E. Public Health and Social Measures

The table highlights changes in public health and social measures (PHSMs) based on data from the Oxford COVID-19 Government Response Tracker. An up arrow indicates new PHSMs were announced; a horizontal arrow indicates PHSM were extended; a down arrow indicates PHSMs were loosened/expired. Member States are organized by tiers based on current epidemiological data from 25th June – 2nd July 2021.

Country	PHSM Trend	PHSM Change
Tier 4 (High Alert): Daily case incidence per 1M people/day ≥ 80 and/or positivity rate ≥ 12%		
Uganda	↑	**Uganda** further tightened COVID-19 restrictions, including a 2-week closure of Parliament and a ban on funeral services.
Cabo Verde	→	Officials in **Cabo Verde** have extended the nationwide state of calamity for an additional 15 days across all islands in the country. Measures include restrictions on the times during which bathing is permitted on beaches, a ban on public and private gatherings, and curfews for bars and restaurants.
South Africa	↑	Authorities in **South Africa** tightened COVID-19 restrictions for 14 days amid increasing transmission. Measures include a ban on all gatherings of any kind, the closure of schools, a nightly curfew, and restrictions on restaurants to take out only.
Namibia	↑	Authorities have tightened COVID-19 restrictions through July 15. All interprovincial travel is prohibited with the exception of essential workers. Authorities have increased the nationwide curfew by one hour. .
Tunisia	↑	The nightly curfew in **Tunisia** has been lengthened by two hours, now from 20:00-5:00. Gatherings of all kinds are also banned until 11 July.
Tier 3 (Moderate Alert): Daily case incidence per 1M people/day is 20 to <80 and/or positivity rate is 5% to <12%		

Rwanda	↑	**Rwanda** announced stricter restrictions due to an intense surge of COVID-19 cases. The nationwide curfew from 6pm to 4am will remain in place. New restrictions in hotspots include bans on all public and private gatherings; school closures; and closures of bars and restaurants.
Zimbabwe	↑	Authorities reimposed lockdown measures nationwide through July 13 due to the rising number of COVID-19 cases, including a strict curfew from 6:30pm to 6am.
Eswatini	↑	Officials in **Eswatini** have instituted controversial new measures, including restrictions on business hours, a nightly curfew, and school closures.
Kenya	→	COVID-19 preventative measures were extended for an additional 60 days in **Kenya**. Measures include a nightly curfew, a ban on public gatherings, and capacity limitations for religious services.
Tier 2 (Low Alert): Daily case incidence per 1M people/day is 5 to <20 and/or positivity rate is 3% to 5%		
Madagascar	→	**Madagascar** extended the national state of emergency for an additional 15 days. A nightly curfew remains in place, from 0:00 to 4:00, and gatherings of more than 400 people are prohibited.
Tier 1 (Standard Precautions): Daily case incidence per 1M people/day is <5 and/or positivity rate is <3%		
Guinea-Bissau	↓	Authorities in **Guinea-Bissau** extended the nationwide state of alert until 8 July, which includes measures such as mandatory use of facemasks in public, capacity restrictions for funeral services, and closure of nightclubs and gyms.
Nigeria	↑	**Nigeria** restricted travel from Uganda, South Africa, Zambia, and Rwanda to prevent transmission of the Delta variant.

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