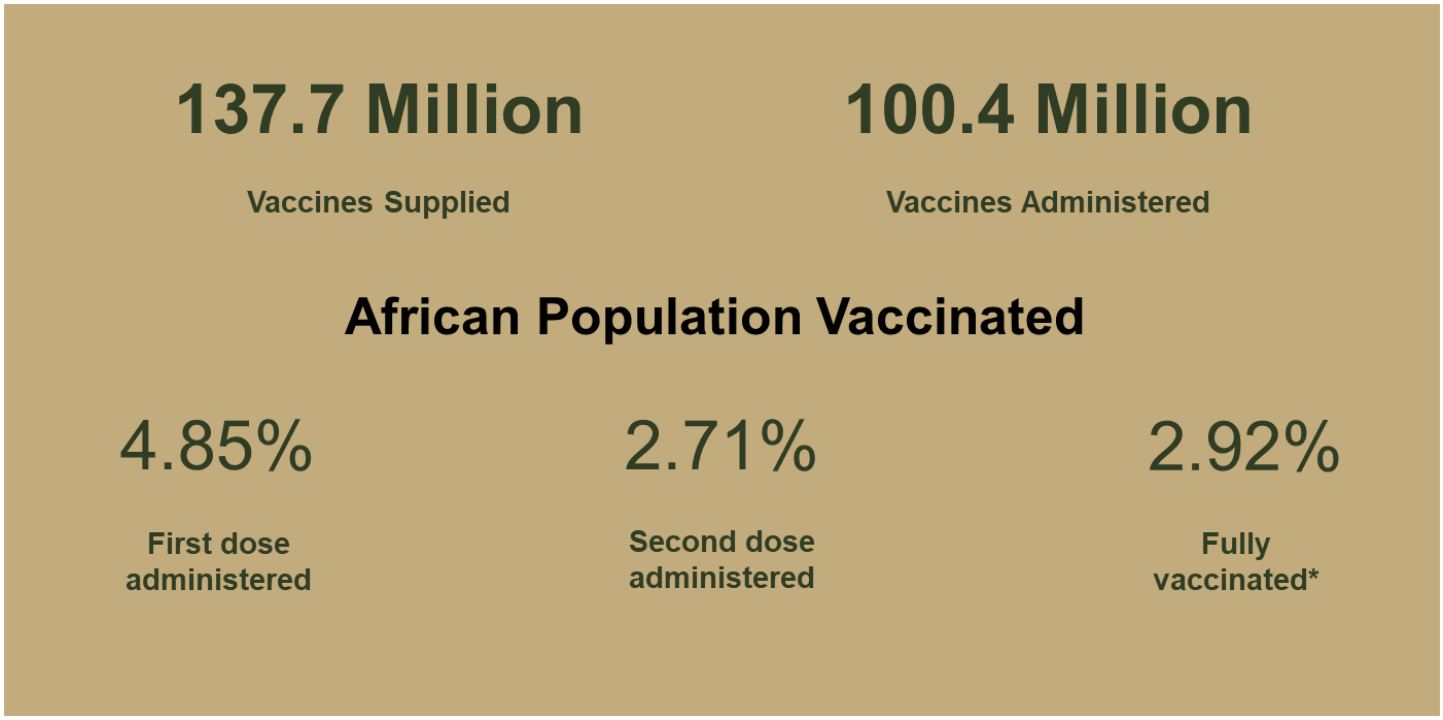
COVID-19 Scientific and Public Health Policy Update[1] – (31 August 2021)

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

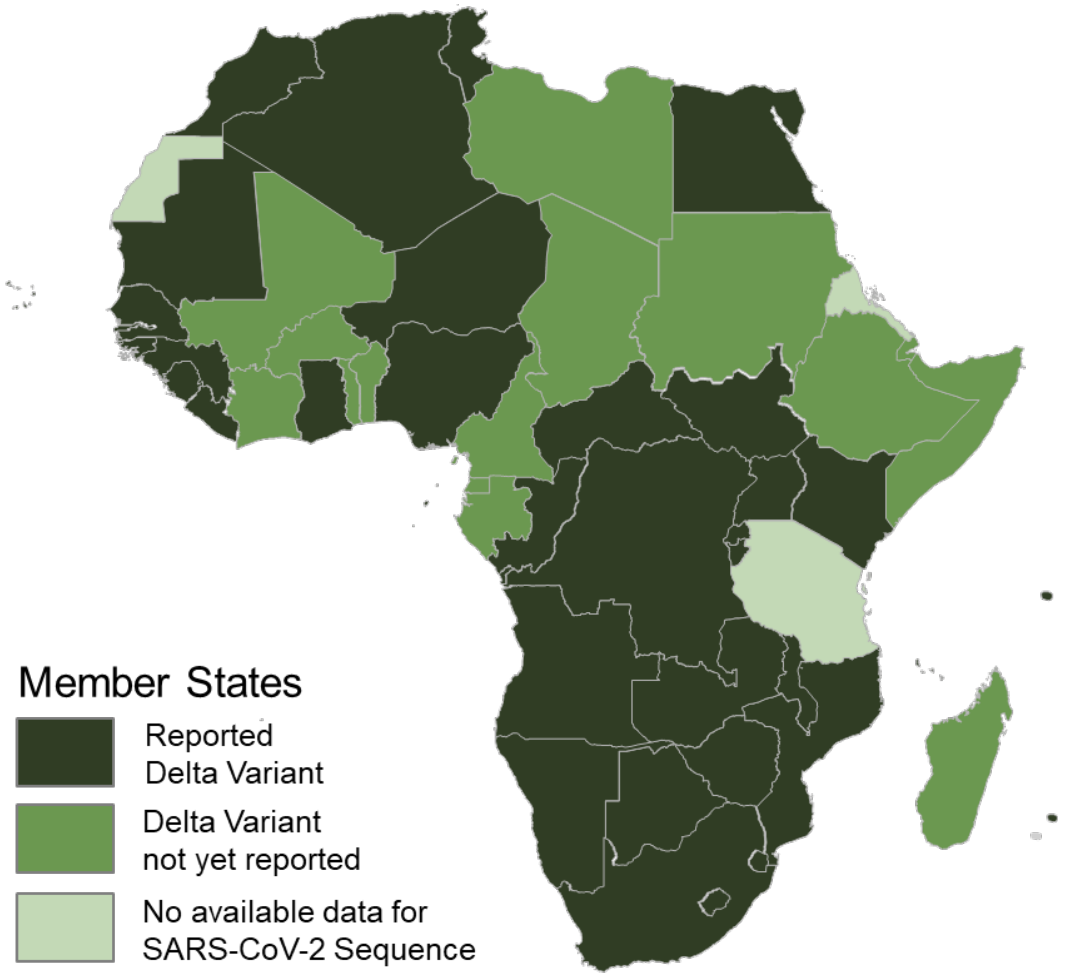


*Received two doses/ one dose of Johnson & Johnson vaccine
https://africacdc.org/covid-19-vaccination/
Updated 31st August 2021

[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**.

Variants of Concern

- The Delta variant (B.1.617.2), first reported in India, has spread to more than 170 countries worldwide; 35 Member States in Africa have reported this variant. https://africacdc.org/institutes/africa-pathogen-genomics-initiative/



Updated 31st August, 2021

B. New guidelines and resources

Since 14th August 2021,

- Africa CDC has published new guidance and resources on:
  - COVID-19 Tiered Public Health and Social Measure Framework for Africa
  - Report: Cross Country Learning on Community Health System Integration and Financing

- US CDC has published new guidance and resources on:
  - What You Should Know About COVID-19 Testing in Schools
  - Interim Public Health Recommendations for Fully Vaccinated People
  - Guidance for General Laboratory Safety Practices during the COVID-19 Pandemic
  - Breastfeeding and Caring for Newborns if You Have COVID-19
  - Documenting Vaccinations at Third-Party Clinics in VAMS

- WHO has published new guidance and resources on:
  - WHO compendium of innovative health technologies for low-resource settings 2021. COVID-19 and other health priorities

  - Digital documentation of COVID-19 certificates: vaccination status: technical specifications and implementation guidance
  - Digital documentation of COVID-19 certificates: vaccination status: web annex A: DDCC:VS core data dictionary
  - Digital documentation of COVID-19 certificates: vaccination status: technical specifications and implementation guidance, web annex B: technical briefing

- FDA has issued press releases on:
  - Joint statement from HHS Public Health and Medical experts on COVID-19 booster shots
  - On 22nd August 2021, the FDA updated the Pfizer-BioNTech emergency use authorization (EUA) to support the extension of shelf-life of the Pfizer-BioNTech COVID-19 Vaccine stored at -90 degrees to -60 degrees Celsius from 6 months to 9 months
  - On 23rd August 2021, FDA approved the first COVID-19 Vaccine
  - As of 27th August 2021, 407 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, 22-28 August, week 34

- PHE has issued new guidance and press releases on:
  - COVID-19 vaccination: myocarditis and pericarditis information for healthcare professionals
  - COVID-19 vaccination: blood clotting information for healthcare professionals
  - COVID-19 vaccination: guide for adults
  - COVID-19 vaccination: Guillain-Barré Syndrome information for healthcare professionals
  - Government data shows mass events can take place safely but fans urged to remain cautious in crowds and get vaccinated
  - Preventing and controlling outbreaks of COVID-19 in prisons and places of detention
  - Guidance for care of the deceased

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

- The authors in this study identified a new SARS-CoV-2 variant assigned to the PANGO lineage C.1.2. This variant has been detected throughout the third wave of infections in South Africa from May 2021 onwards and has been detected in seven other countries in Europe, Asia, Africa and Oceania. C.1.2 contains multiple substitutions (R190S, D215G, E484K, N501Y, H655Y and T859N) and deletions (Y144del, L242-A243del) within the spike protein, which have been observed in other variants of concern (VOCs) and are associated with increased transmissibility and reduced neutralization sensitivity. Furthermore, the variant has accumulated additional mutations (C136F, Y449H and N679K) which are also likely to impact neutralization sensitivity or furin cleavage and therefore replicative fitness. The authors recommend further studies to assess the impact of the variant on antibody neutralization following SARS-CoV-2 infection or vaccination. [*not peer reviewed*]
- This post-mortem study of a 14-month-old child describes the histopathological findings of SARS-CoV-2 infection complicated by neuroinvasion. The authors found several lesions including microthrombosis, pulmonary congestion, interstitial oedema, lymphocytic infiltrates, bronchiolar injury, collapsed alveolar spaces, cortical atrophy, and severe neuronal loss. They observed SARS-CoV-2 staining along the apical region of the choroid plexus (ChP) epithelium and in ependymal cells of the lateral ventricle, but was restricted to ChP capillaries and vessels in some regions. They confirmed SARS-CoV-2 infection of brain tissue by RT-qPCR in fragments of the ChP, lateral ventricle, and cortex.

Their findings suggest that SARS-CoV-2 may invade the central nervous system by blood-cerebrospinal fluid barrier disruption.

- In this drug repurposing study, the authors screened a library of 1900 clinically safe drugs against OC43, a human beta coronavirus that causes the common cold, and evaluated the top hits against SARS-CoV-2. The authors found 20 drugs that significantly inhibited replication of both viruses in cultured human cells. Eight of the drugs inhibited the activity of the SARS-CoV-2 main protease, 3CLpro, with the most potent being masitinib, an orally bioavailable tyrosine kinase inhibitor. X-ray crystallography and biochemistry show that masitinib acts as a competitive inhibitor of 3CLpro. Mice infected with SARS-CoV-2 and then treated with masitinib showed >200-fold reduction in viral titers in the lungs and nose, as well as reduced lung inflammation. Masitinib was also effective in vitro against all tested variants of concern (B.1.1.7, B.1.351, and P.1). They recommend further efforts to evaluate the efficacy of masitinib in treating COVID-19 patients.
- This study aimed to investigate how expression of viral entry and cell death genes in the lung might vary among different age groups and how this variation relates to known differences in disease severity. The authors used human lung specimens from more than 100 donors along with transcriptional profiling and live virus experiments to define novel correlates of COVID-19 disease severity and demonstrated that apoptosis, whether modulated physiologically or pharmacologically, can modulate cellular responses to SARS-CoV-2 infection and potentially curtail viral production.
- In this in vivo study, the authors generated nucleoside-modified mRNA-lipid nanoparticle (LNP) vaccines expressing chimeric spikes that contain admixtures of different receptor binding domain (RBD), N-terminal domain (NTD), and subunit 2 (S2) modular domains from zoonotic, epidemic, and pandemic coronaviruses and examined their efficacy against homologous and heterologous Sarbecovirus challenge in aged mice. The chimeric vaccines protected against challenge from SARS-CoV, SARS-CoV-2 and tested variants of concern, and zoonotic coronaviruses with pandemic potential. They recommend further studies to determine whether other combinations of chimeric mRNA-LNP vaccines from other SARS-like viruses are protective, elicit broad T cell responses, prevent the rapid emergence of escape viruses, elicit protective responses in nonhuman primate models of Sarbecovirus pathogenesis, and can boost Sarbecovirus protective breadth in SARS-CoV-2–vaccinated or convalescent individuals.
- In this prospective cohort study of 292 patients with stage III and IV melanoma, half of which were treated with immune checkpoint inhibitors (ICIs), the authors characterised the clinical expression of COVID-19 and monitored the development of anti–SARS-CoV-2 antibodies. They identified 15 patients with acute or convalescent COVID-19 and investigated their transcriptomic, proteomic, and cellular profiles. They found that ICI treatment was not associated with severe COVID-19 and did not alter the induction of inflammatory and type I interferon responses. In-depth phenotyping demonstrated expansion of CD8 effector memory T cells, enhanced T cell activation, and impaired plasmablast induction in ICI-treated COVID-19 patients. The evaluation of specific adaptive immunity in convalescent patients showed higher spike (S), nucleoprotein (N), and membrane (M) antigen-specific T cell responses and similar induction of spike-specific antibody responses. Their findings provide evidence that ICI during COVID-19 enhanced T cell immunity without exacerbating inflammation.

Vaccines

- This retrospective cohort study compared the incidence rates of breakthrough infections to the incidence rates of re-infection in Israel when the Delta variant was dominant. The study involved 3 groups: (1) SARS-CoV-2-naïve individuals who received a two-dose regimen of the BNT162b2 vaccine, (2) previously infected individuals who have not been vaccinated, and (3) previously infected *and* single dose vaccinated individuals. Their results show that SARS-CoV-2-naïve vaccinees had a 13.06-fold (95% CI, 8.08 to 21.11) increased risk for breakthrough infection with the Delta variant compared to those previously infected. The increased risk was significant for symptomatic disease as well. Their study demonstrated that natural immunity confers longer lasting and stronger protection against infection, symptomatic disease and hospitalization caused by the Delta variant of SARS-CoV-2, compared to the BNT162b2 two-dose vaccine-induced immunity. Individuals who were both

previously infected with SARS-CoV-2 and given a single dose of the vaccine gained additional protection against the Delta variant. [*not peer reviewed*]

- This prospective cohort study of 17,525 adults aimed to investigate experiences of pregnant and lactating individuals after receiving COVID-19 vaccines. The cohort included 3 distinct groups: 7809 individuals who were pregnant (44.6%), 6815 individuals who were lactating (38.7%), and 2901 individuals who were neither pregnant nor lactating but planning pregnancy in the near future (16.5%) at the time of their first vaccine dose. Most individuals received the BNT162b2 vaccine (61.9%) or mRNA-1273 vaccine (37.8%). Majority of the participants (85.9%) reported receiving 2 doses. Among all participants, 17,005 individuals (97.0%) reported any post vaccination reactions after the first dose, with the most common reactions being pain at injection site (91.4%) and fatigue (31.3%). The frequency of reactions after the second dose was higher than after the first dose, but with similar distribution of symptoms. Odds of several reactions were statistically significantly decreased among individuals who were pregnant compared with individuals who were neither pregnant nor lactating. Among pregnant participants, any obstetrical symptoms were reported by 346 of 7809 individuals (4.4%) after the first dose and 484 of 6444 individuals (7.5%) after the second dose. This study found that COVID-19 vaccines were well-tolerated among individuals who were pregnant, lactating, or planning pregnancy.
- This study analysed observational data from Clalit Health Services (CHS) in order to emulate a target trial of the effects of the BNT162b2 vaccine on a broad range of potential adverse events in a population without SARS-CoV-2 infection. The data set included more than 2.4 million vaccinated persons in Israel. The authors derived risk ratios and risk differences at 42 days after vaccination with the use of the Kaplan–Meier estimator. They performed a similar analysis involving SARS-CoV-2–infected persons matched to uninfected persons. They found that BNT162b2 vaccine was not associated with an elevated risk of most of the adverse events examined. The vaccine was associated with an excess risk of myocarditis (1 to 5 events per 100,000 persons). The risk of this potentially serious adverse event and of many other serious adverse events was substantially increased after SARS-CoV-2 infection. Their findings help to shed light on the short- and medium-term risks of the vaccine and place them in clinical context. They recommend further studies to estimate the potential of long-term adverse events.
- This cross-sectional study aimed to determine the level and determinants of COVID-19 vaccine hesitancy in Kenya. The authors administered a phone-based survey among 4136 respondents in February 2021 in four counties of Kenya (Kilifi, Kisumu, Nairobi and Wajir). They found a high COVID-19 vaccine hesitancy (36.5%). Factors associated with vaccine hesitancy included: Rural regions (aOR:2.46; 95% CI:1.02–5.94), perceived difficulty in adhering to government regulations on COVID-19 prevention (aOR:1.96; 95%CI:1.65–2.33), no perceived COVID-19 infection risk (aOR:1.80; 95% CI:1.54–2.10), concerns regarding vaccine safety and effectiveness (aOR:3.38; 95% CI:2.81–4.07), and religious and cultural reasons (aOR:1.42; 95% CI:1.01–1.98). They recommend the prioritization of interventions to address vaccine hesitancy and improve vaccine confidence as part of the vaccine roll-out plan. The messaging and/or interventions should be holistic to include the value of other public health measures, be focused and targeted to specific groups, raise awareness on the risks of COVID-19 and effectively communicate the benefits and risks of vaccines.
- The authors in this study conducted a correlational analysis using vaccination coverage and mutation frequency of the SARS-CoV-2 Delta variant in 16 countries. They found a strong inverse relationship (R2=0.878), indicating that universal vaccination against COVID-19 is critical to suppress emergent mutations. They also recommend the urgent re-implementation of non-pharmaceutical measures i.e masking and social distancing, to monitor for new mutations through genomic surveillance. Furthermore, they present a tool to forecast new COVID-19 outbreaks [*not peer reviewed*]
- This study aimed to evaluate whether convalescent sera and sera from vaccine recipients are similarly affected in their ability to neutralize authentic virions. The authors analysed antibodies and T cells of a recently vaccinated, UK cohort, alongside those recovering from natural infection in early 2020. Their results show that neutralization of the variants of concern (VOC) compared to a reference isolate of the original circulating lineage, B, is reduced: more profoundly against B.1.351 than for B.1.1.7, and in responses to infection or a single dose of vaccine than to a second dose of vaccine. High magnitude T cell responses are generated after two vaccine doses, with the majority of the T cell response directed

against epitopes that are conserved between the prototype isolate B and the VOC. Their findings re-emphasise the urgent need to deploy the most effective vaccine strategies as widely and rapidly as possible in order to provide population protection against the emerging lineages of concern of SARS-CoV-2.

- This study reports on the use of an analytics-based approach to identify and contact marginalized patients who might benefit from targeted non-electronic communication regarding COVID-19 immunization. The authors identified 536 potentially marginalized patients who received cancer therapy during the past year with follow-up scheduled, without an active patient portal account, no valid email on file, or who lived in a county with a greater than 20% poverty rate across multiple census points in North Carolina who were eligible for COVID-19 vaccination. Nearly all identified patients were called (>99%), with 350 (67%) successfully reached and 46 (9%) who received voicemails. The mean (SD) duration of phone calls was 4.3 (4.1) minutes. As of April 2, 2021, 93 of 359 contacted patients (26%) were confirmed to have received vaccination via electronic health record review or self-report, with another 14 of 359 (4%) scheduled for a vaccination appointment. This study demonstrated the potential benefits of an analytics-based strategy to reach marginalized patients at high risk for exclusion from outreach vaccination programs.
- This longitudinal study evaluated symptoms following vaccination and serum spike antibody levels in a cohort of hospital workers (HWs) who received either mRNA vaccine and had known status of prior SARS-CoV-2 infection to identify differences in symptoms and serum immunoglobulin G (IgG) antibodies against S1 spike protein. A questionnaire and serum sample were collected 14 or more days following dose 2 for 954 HWs. Clinically significant symptoms were reported by 52 of the 954 (5%) after dose 1 and 407 (43%) after dose 2. Clinically significant symptoms following dose 1 were associated with prior SARS-CoV-2 infection, confirming prior reports. Nearly 100% of HWs in this study mounted a strong antibody response to the spike protein after dose 2 of the SARS-CoV-2 mRNA vaccine independent of vaccine-induced reactions. Spike IgG antibody measurements were higher in HWs who received the Moderna vaccine, had prior SARS-CoV-2 infection, and reported clinically significant reactions. Their findings suggest that regardless of vaccine reactions or prior SARS-CoV-2 infection, either spike mRNA vaccine will provide a robust spike antibody response.
- This study investigated whether vaccination would reduce transmission in the household setting in the context of post vaccination infection. The authors analysed multiple secondary datasets in England. They compared the risk of secondary infection among unvaccinated household contacts of persons with SARS-CoV-2 infection who had received at least one dose of the ChAdOx1 nCoV-19 or BNT162b2 vaccine 21 days or more before testing positive with the risk among unvaccinated household contacts of unvaccinated persons with infection. Between January 4 and February 28, 2021, there were 960,765 household contacts of unvaccinated index patients, and there were 96,898 secondary cases of COVID-19 (10.1%). The likelihood of household transmission was approximately 40 to 50% lower in households of index patients who had been vaccinated 21 days or more before testing positive than in households of unvaccinated index patients; the findings were similar for the two vaccines. Most of the vaccinated index patients (93%) had received only the first dose of vaccine. Assessment of infection risks among household contacts according to the timing of vaccination of the index patient showed protective effects when the vaccine had been administered at least 14 days before the positive test.
- This study aimed to investigate the possibility of a cross-clade boost of broad-spectrum neutralizing antibodies in survivors of SARS-CoV-1 infection in Singapore who had received the BNT162b2 mRNA vaccine against SARS-CoV-2. Their findings show the efficient induction of high-level and broad-spectrum pan-sarbecovirus neutralizing antibodies that can neutralize all variants of concern and five sarbecoviruses that have been identified in bats and pangolins and that have the potential to cause human infection. Their study showed the feasibility of achieving pan-sarbecovirus neutralization through cross-clade boosting in humans that was more uniform and stronger than that observed in animals.
- This exploratory study aimed to evaluate public trust in information sources, confidence in institutions and COVID-19 vaccine willingness in Trinidad and Tobago. An online survey was conducted from 10th November to 7th December 2020 using a validated questionnaire developed by WHO and adapted to the local setting. The authors found that the most trusted sources of information included health workers

(32.5%) and the ministry of health (23.6 %). Increasing levels of trust in the medical sector were associated with decreasing levels of believing misinformation. Overall, 62.8 % of participants said they would take the COVID-19 vaccine if available. Regression analyses showed those who agreed that everyone should adhere to the national immunization schedule and those who would take the flu vaccine, were 2.77 (95% CI 1.77-4.35) and 4.60 (95% CI 3.11-6.84) times more likely to take the vaccine, respectively. Their results may guide public health response activities and identify areas for prioritisation and improvement.

- This test negative case-control study aimed to estimate the effectiveness of the inactivated whole virus vaccine, CoronaVac (Sinovac Biotech), against symptomatic COVID-19 in the elderly population of São Paulo state, Brazil during widespread circulation of the gamma variant. The study involved adults aged ≥70 years. The authors formed 13,283 matched sets, one case with to up to five controls, according to age, sex, self-reported race, municipality of residence, previous COVID-19 status, and date of RT-PCR test (±3 days). Their findings show that, the adjusted vaccine effectiveness against symptomatic COVID-19 was 24.7% (95% CI 14.7% to 33.4%) at 0-13 days and 46.8% (38.7% to 53.8%) at ≥14 days after the second dose. Adjusted vaccine effectiveness against hospital admissions was 55.5% (46.5% to 62.9%) and against deaths was 61.2% (48.9% to 70.5%) at ≥14 days after the second dose. Vaccine effectiveness ≥14 days after the second dose was highest for the youngest age group (70-74 years) 59.0% (43.7% to 70.2%) against symptomatic disease, 77.6% (62.5% to 86.7%) against hospital admissions, and 83.9% (59.2% to 93.7%) against deaths. Vaccine effectiveness was observed to decline with increasing age.

Diagnostics

- This multicentre prospective observational study of diagnostic accuracy aimed to evaluate the intrinsic and extrinsic performances of a colorimetric reverse transcription loop-mediated isothermal amplification (RT-LAMP) in resource-limited settings. The study was conducted from October 2020 to February 2021 in Cameroon, Ethiopia, Kenya, Nigeria and Italy. The authors enroled 1657 individuals who were either COVID-19 suspect cases, or asymptomatic and presented for screening. RNA extracted from pharyngeal swabs was tested in parallel by a colorimetric RT-LAMP and by a standard real time polymerase chain reaction (RT-PCR). For a subset of 1292 specimens, which underwent exactly the same procedures in different countries, the authors obtained very high specificity (98%) and positive predictive value (PPV = 99%), while the sensitivity was 87%, with a negative predictive value NPV = 70%, Stratification of RT-PCR data showed superior sensitivity achieved with an RT-PCR cycle threshold (Ct) below 35 (97%), which decreased to 60% above 35. These results show that, RT-LAMP appears to be a reliable assay, comparable to RT-PCR, particularly with medium-high viral loads (Ct < 35) and can be deployed in resource-limited settings for timely management and prevention of COVID-19, without compromising the quality of output.
- This study describes implementation of high-frequency testing using inexpensive, at-home, semi quantitative, direct antigen rapid tests (DARTs) and compare their performance with that of qRT-PCR on self-collected nasal specimens. The cohort study enrolled 257 participants from 3 laboratories in Cambridge and Boston, Massachusetts. The prevalence of COVID-19 in the area during the study was between less than 1% and 8%. A total of 2951 pairs of nasal swabs were self-collected over the course of 6 months. The authors found that twice-weekly surveillance with DART detected infections in 15 individuals, with 96.3% sensitivity on days 0 through 3 of symptoms. The sensitivity of DART within days 0 to 12 of symptom onset was 78.9% (60 of 76 swabs; 95% CI, 69.1%-88.8%), and the specificity of DART was 97.1% (2791 of 2875 swabs; 95% CI, 96.3%-97.8%). Frequent at-home testing with DART allows infected individuals to be identified and quarantined immediately. Such surveillance can prevent viral transmission in in-person work environments or other social settings.

Care and Treatment

- This cohort study aimed to determine whether patients with cancer treated with potential ACE2-lowering antineoplastic compounds exhibit lower SARS-CoV-2 infection rates. The authors performed an in silico analysis of the Library of Integrated Network-Based Cellular Signatures database and identified 91 antineoplastic compounds associated with decreased angiotensin-converting enzyme 2 (*ACE2*) gene expression across cell lines, including mTOR/PI3K inhibitors (everolimus, temsirolimus, and alpelisib) and antimetabolites (decitabine and gemcitabine). Patients who received a potential ACE2-lowering antineoplastic exhibited a statistically significantly reduced SARS-CoV-2 positivity rate of 7.0% compared with 12.9% in patients who received other antineoplastic therapies. The authors recommend further evaluation of the biological and clinical anti–SARS-CoV-2 properties of identified antineoplastic compounds.
- This randomised, multicentre, single-blind trial aimed to evaluate whether the infusion of convalescent plasma containing high titers of neutralizing antibodies would prevent progression to severe COVID-19. The authors randomised 511 high-risk patients, who presented to the emergency department within 7 days after the onset of COVID-19 symptoms, in a 1:1 ratio to receive an infusion of either one unit of ABO-compatible COVID-19 convalescent plasma or 250 ml of placebo. The primary outcome was disease progression within 15 days after randomization, which was a composite of hospital admission for any reason, seeking emergency or urgent care, or death without hospitalization. Their results show that the administration of COVID-19 convalescent plasma to high-risk outpatients within 1 week after the onset of symptoms did not prevent disease progression.
- This open-label, adaptive, multiplatform, randomised clinical trial 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 intensive care unit (ICU)–level cardiovascular or respiratory organ support in critically ill patients with COVID-19. The trial was stopped when the prespecified criterion for futility was met for therapeutic-dose anticoagulation. Data on the primary outcome were available for 1098 patients (534 assigned to therapeutic-dose anticoagulation and 564 assigned to usual-care thromboprophylaxis). Their results show that an initial strategy of therapeutic-dose anticoagulation with heparin did not result in a greater probability of survival to hospital discharge or a greater number of days free of cardiovascular or respiratory organ support than did usual-care pharmacologic thromboprophylaxis in critically ill patients with COVID-19.
- This systematic review and meta-analysis aimed to assess the effectiveness of specific interleukin inhibitors for the treatment of COVID-19. The authors searched electronic databases to identify studies on immunomodulatory agents (anakinra, sarilumab, siltuximab and tocilizumab) and included 71 studies totalling 22,058 patients. Most studies explored outcomes in patients who received tocilizumab (60/71). In prospective studies, tocilizumab was associated with improved unadjusted survival (risk ratio 0.83, 95% CI 0.72 to 0.96, I^2=0.0%), but conclusive benefit was not demonstrated for other outcomes. In retrospective studies, tocilizumab was associated with less severe outcomes on an Ordinal Scale (generalised OR 1.34, 95% CI 1.10 to 1.64, I^2=98%) and adjusted mortality risk (HR 0.52, 95% CI 0.41 to 0.66, I^2=76.6%). Their results demonstrate that tocilizumab is associated with lower mortality in COVID-19. They recommend further exploration of other immunomodulatory therapies.

Epidemiology

- This study aimed to investigate the spatial invasion dynamics of lineage B.1.1.7 by jointly analysing UK human mobility, virus genomes, and community-based polymerase chain reaction data. The authors identified a multistage spatial invasion process in which early B.1.1.7 growth rates were associated with mobility and asymmetric lineage export from a dominant source location, enhancing the effects of B.1.1.7's increased intrinsic transmissibility. They further explored how B.1.1.7 spread was shaped by non-pharmaceutical interventions and spatial variation in previous attack rates. Their findings show that careful accounting of the behavioural and epidemiological context within which variants of concern emerge is necessary to interpret correctly their observed relative growth rates.
- This study aimed to investigate global SARS-CoV-2 genomic surveillance during the first 15 months of COVID-19 pandemic. The authors provide a spatial and temporal perspective on the global disparities

surrounding SARS-CoV-2 genomic surveillance, their causes and consequences, and possible solutions to maximise the impact of pathogen genome sequencing for efforts on public health. [*not peer reviewed*]

- This cohort study aimed to characterise the severity of the delta variant compared with the alpha variant by determining the relative risk of hospital attendance outcomes among 43,338 COVID-19 patients in England. The authors found a higher hospital admission or emergency care attendance risk for patients with COVID-19 infected with the delta variant compared with the alpha variant (adjusted HR 1.45 [1.08–1.95]). Their results suggest that outbreaks of the delta variant in unvaccinated populations might lead to a greater burden on health-care services than the alpha variant.
- This ambidirectional cohort study aimed to comprehensively compare consequences between 6 and 12 months after symptom onset among hospital survivors with COVID-19. The study involved 1276 COVID-19 survivors who had been discharged from Jin Yin-tan Hospital (Wuhan, China) between Jan 7 and May 29, 2020. The proportion of patients with at least one sequelae symptom decreased from 68% (831/1227) at 6 months to 49% (620/1272) at 12 months (p<0·0001). They found that most patients had a good physical and functional recovery during follow-up, and the majority of study participants who were employed before COVID-19 had returned to their original work. However, sequelae symptoms, lung diffusion impairment, and radiographic abnormalities persisted to 12 months in some patients, especially in patients who were critically ill during hospital stay. The health status of the cohort was still lower than that in the control population.
- This secondary data analysis on deaths registered on the National Population Register by the Department of Home Affairs in South Africa (SA) aimed to quantify the excess deaths and likely magnitude of COVID-19 in SA in 2020 and draw conclusions on monitoring the epidemic in 2021. The authors calculated excess deaths by comparing the weekly number of deaths with the number predicted based on the Holt-Winters time series analysis of past deaths. They estimated a 13% increase in the number of deaths in 2020. The excess death rate from natural causes was 122 per 100 000 population, with a male-to-female ratio of 0.78. Deaths from unnatural causes halved for both males and females during the stringent lockdown level 5. The numbers reverted towards the predicted number with some fluctuations as lockdown restrictions varied. Just under 5,000 unnatural deaths were averted. Their findings highlight that the ~28 000 reported COVID-19 deaths during 2020 substantially understate the death toll from the pandemic by a factor of 2.7. They recommend an improvement of the cause-of death information system so that it can inform public health actions timely.
- This modelling study aimed to examine the potential epidemiological and evolutionary impacts of 'vaccine nationalism': stockpiling vaccines to prioritise rapid access to their citizenry. The authors incorporated vaccine sharing scenarios in two countries whose infection dynamics are either otherwise independent or coupled through immigration of infectious individuals and evolution-driven increases in transmission rates. They found that when vaccines are widely available and the immunity they confer is robust, sharing doses minimizes total cases across regions. Asymmetries in population size or transmission rates introduce additional complexities, which are particularly marked when natural and vaccine-induced immunity is weak. Sustained transmission in low access regions results in an increased potential for antigenic evolution, which may result in the emergence of novel variants that affect epidemiological characteristics globally. Their results stress the importance of rapid equitable vaccine distribution for global control of the pandemic.
- This systematic review and meta-analysis aimed to use newly published data to further the understanding of SARS-CoV-2 transmission in the household. The authors included 87 studies representing 1,249,163 household contacts from 30 countries. The estimated household secondary attack rate (SAR) was 18.9% (95% CI, 16.2%-22.0%). Compared with studies from January to February 2020, the SAR for studies from July 2020 to March 2021 was higher (13.4% [95% CI, 10.7%-16.7%] vs 31.1% [95% CI, 22.6%-41.1%], respectively). The SAR was higher to contacts with comorbidities (3 studies; 50.0% [95% CI, 41.4%-58.6%]) compared with previous findings, and the estimated household SAR for the B.1.1.7 (α) variant was 24.5% (3 studies; 95% CI, 10.9%-46.2%). The findings of this study suggest that the household remains an important site of SARS-CoV-2 transmission, and recent studies have higher household SAR estimates compared with the earliest reports. More transmissible variants and vaccines may be associated with further changes.

- This cohort study aimed to investigate the association between the timing of exposure and development of disease among close contacts of index patients with COVID-19 and to evaluate whether the severity of the index case is associated with clinical presentation in close contacts who develop COVID-19. The study included 730 index patients in Zhejiang Province, China, from January 8 to July 30, 2020 along with their 8852 close contacts. The authors found that contacts were at highest risk of COVID-19 if they were exposed between 2 days before and 3 days after the index patient's symptom onset, peaking at day 0 (adjusted relative risk [ARR], 1.3; 95% CI, 1.2-1.5). Compared with being exposed to an asymptomatic index patient, the risk of COVID-19 among contacts was higher when they were exposed to index patients with mild (ARR, 4.0; 95% CI, 1.8-9.1) and moderate (ARR, 4.3; 95% CI, 1.9-9.7) cases of COVID-19. As index case severity increased, infected contacts were less likely to be asymptomatic (exposed to patient with mild COVID-19: ARR, 0.3; 95% CI, 0.1-0.9; exposed to patient with moderate COVID-19: ARR, 0.3; 95% CI, 0.1-0.8). Their results suggest that the quantity of exposure to a patient with COVID-19 may be associated with clinical presentation among close contacts who develop COVID-19.
- This study describes the epidemiology of COVID-19 in South Africa following importation and during implementation of stringent lockdown measures. The authors used national surveillance data from 4 March to 30 April 2020, to generate and interpret descriptive statistics, epidemic curves, and initial reproductive numbers. A total of 271,670 SARS-CoV-2 PCR tests were performed (462 tests/100,000 persons), of which, 7,892 (2.9%) persons tested positive (median age 37 years (IQR 28–49 years), 4,568 (58%) male. Their findings show that, the first 8 weeks following COVID-19 importation were characterised by early predominance of imported cases and relatively low mortality and transmission rates. The second month following importation was characterised by community transmission and increasing disease burden in more populous provinces despite the stringent lockdown measures.
- This population-based cohort study aimed to determine whether there are differences in the odds of household transmission by younger children compared with older children. The study was conducted between June 1 and December 31, 2020, in Ontario, Canada. The authors report that a total of 6280 households had paediatric index cases, and 1717 households (27.3%) experienced secondary transmission. Children aged 0 to 3 years had the highest odds of transmitting SARS-CoV-2 to household contacts compared with children aged 14 to 17 years (OR, 1.43; 95% CI, 1.17-1.75). Children aged 4 to 8 years and 9 to 13 years also had increased odds of transmission (aged 4-8 years: OR, 1.40; 95% CI, 1.18-1.67; aged 9-13 years: OR, 1.13; 95% CI, 0.97-1.32). Their results suggest that younger children may be more likely to transmit SARS-CoV-2 infection compared with older children. Differential infectivity of paediatric age groups has implications for infection prevention within households, as well as schools/childcare, to minimize risk of household secondary transmission.

Infection Prevention and Control

- In this review, the authors discuss current evidence regarding the transmission of respiratory viruses by aerosols, how they are generated, transported, and deposited, as well as the factors affecting the relative contributions of droplet-spray deposition versus aerosol inhalation as modes of transmission. The authors suggest that airborne transmission may be the dominant form of transmission for several respiratory pathogens, including SARS-CoV-2, and that further understanding of the mechanisms underlying infection from the airborne route will better inform mitigation measures.
- This retrospective observational study analysed the nosocomial COVID-19 cases that occurred in healthcare workers and inpatients and their caregivers in a tertiary care hospital in Korea. The authors identified 21 nosocomial events involving 65 individuals with COVID-19. They found that infectors tended to have a longer duration between symptom onset and diagnostic confirmation than did the non-infectors (median 2 days vs. 0 days, P = 0.08). Approximately 70% of the nosocomial cases of COVID-19 did not generate secondary cases. They identified 12 individuals who were responsible for multiple-spreading events and 1 for a super-spreading event, which collectively generated 35 secondary cases. They recommend early case identification, isolation, and extensive contact tracing to prevent transmission and super-spreading events.

Non-pharmaceutical interventions, social distancing

- This prospective cohort study of patients and residents who received direct care from a Healthcare Worker (HCW) with laboratory-confirmed COVID-19 aimed to determine the risk of transmission in the presence of universal masking. The authors report that 3 (2.3%, 95% CI, 0.77-6.4) patients became positive for SARS-CoV-2 among the 133 patients followed up for at least 14 days. Their results provide evidence that universal masking, embedded with other infection control practices, is associated with low risk of transmission of SARS-CoV-2 from healthcare workers to patients and residents.
- This cohort study aimed to examine the association of COVID-19 mitigation measures with changes in cardiorespiratory fitness (CRF) measures and body mass index (BMI) among primary school children. The study included 764 primary schoolchildren aged 7 to 10 years from 12 randomly selected primary schools in urban and rural districts of Klagenfurt, Austria. CRF was measured with a 6-minute endurance run test. Baseline CRF and BMI measurements were obtained in September 2019 before COVID-19 mitigation measures were implemented, and follow-up measurements were obtained in June and September 2020. The authors found that CRF standard deviation (SD) scores changed by −1.06 (95% CI, −1.13 to −1.00), with a similar decrease in both boys and girls. Body mass index SD scores had increased by 0.12 (95% CI, 0.06-0.16) in June 2020 and by 0.16 (95% CI, 0.12-0.20) in September 2020 compared with September 2019. The increase in BMI SD scores was greater among boys than among girls. During the 1-year period, the percentage of children with overweight or obesity increased from 20.3% to 24.1%. Their findings suggest that collaborative efforts are needed to improve children's health and fitness to prevent long-term negative health outcomes.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 27th August 2021, the National Institutes of Health (NIH) reported the launching of a clinical trial to evaluate an additional or booster shot of an authorised or approved Covid-19 vaccine in autoimmune disease patients in the United States. The trial will assess the antibody response in patients who had no response to an original vaccine regimen against SARS-CoV-2 and also the pausing immunosuppressive therapy for autoimmune disease to improve antibody response to an additional dose of a COVID-19. An approximate of 600 participants aged 18 years and older at 15 to 20 sites in the US will be enrolled. Preliminary results are expected in November 2021. Clinical trial registration #: NCT05000216
- On 26th August 2021, INOVIO announced that it has received regulatory authorization from Brazil to initiate the universal phase 3 segment of the INNOVATE Phase 2/3 trial for its deoxyribonucleic acid (DNA) vaccine candidate, INO-4800, for COVID-19. The trial will evaluate the efficacy of INO-4800 in a two-dose regimen (2.0 mg per dose), administered one month apart in 18 years of age and older healthy adults. This randomized clinical study will be carried out in several countries across Latin America, Asia, and Africa. The primary endpoint of this case-driven Phase 3 trial is virologically confirmed COVID-19. Clinical trial registration #: NCT04447781
- On 26th august 2021, the United Kingdom Health Security Agency (UKHSA) announced that it will lead a consortium of academic partners to understand why some people become infected after vaccination or prior infection while others do not. The consortium will use participants from various ongoing studies including SIREN, PITCH, HICC, G2P, GenOMICC and the Francis Crick Institute to assess their detailed immune system response to COVID-19 infections and vaccination. They will also analyze their genetic code, to see if there are any particular mutations in their DNA that might predict a poor response to vaccination.
- On 25th August 2021, Moderna announced that it has completed submission of Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) for its COVID 19 vaccine and has requested FDA Priority Review designation. The FDA Fast-Track designation in May 2020 allowed Moderna to submit Phase 3 COVE clinical study data on a rolling basis in June 2021. Moderna COVID-19 vaccine is currently permitted for use to individuals 18 years of age and older under an

Emergency Use Authorization. However, the company has applied for revision to EUA to include adolescent between 12 to 17 years of age.

- On 25th August 2021, Johnson & Johnson reported data supporting the use of its COVID-19 vaccine as a booster shot for people previously vaccinated with the single-shot Johnson & Johnson vaccine. The company had conducted two Phase 1/2a studies to determine the potential need for boosters. Preliminary results from the studies have demonstrated that a booster dose of Johnson & Johnson COVID-19 vaccine had generated a nine-fold rapid and robust increase in spike-binding antibodies 28 days after primary single-dose vaccination. These were observed in participants between ages 18 and 55, and in those 65 years and older who had received a lower booster dose. Clinical trial registration #: NCT04889209
- On 25th August 2021, Pfizer and BioNTech announced that they have initiated a supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) for the approval of a booster (third) dose of a COVID-19 mRNA vaccine, COMIRNATY®, to prevent COVID-19 in individuals 16 years of age and older. This comes after phase 3 data showed that the booster (third) dose of COMIRNATY induced significant SARS-CoV-2 neutralizing antibody titers and also demonstrated a favorable safety and tolerability profile of COMIRNATY®. The companies intend to complete submission of the sBLA by the end of August.
- On 24th August 2021, United Kingdom government announced the launching of a new clinical trial, OCTAVE DUO, to evaluate the ability of a third Covid-19 vaccine dose to improve the immune response for people who have weakened immune systems. People who are immunosuppressed or immunocompromised will be inoculated with either a Pfizer, Moderna or Novavax vaccine and determine whether a stronger immune response than 2 doses will be developed. The trial will also assess the durability of vaccine protection. Preliminary results are expected later this year.
- On 24th August 2021, Gennova Biopharmaceuticals reported positive preliminary clinical data of the phase I study of its first COVID-19 mRNA vaccine, HGCO19, which is being developed in partnership with DBT-BIRAC under Mission COVID Suraksha. Preliminary results show that HGCO19 vaccine is safe, tolerable, and immunogenic in participants of the study. Following this, an approval to conduct a prospective, multicenter, randomized, active-controlled, observer-blind phase II/III clinical trial was granted. Phase II/III study will be conducted at 10-15 sites in Phase II and 22-27 sites in Phase III in India.
- On 23rd August 2021, Pfizer and BioNTech announced that U.S. Food and Drug Administration (FDA) has approved their Biologics License Application (BLA) for their Covid-19 messenger ribonucleic acid (mRNA) vaccine, COMIRNATY®, to prevent the disease in individuals aged 16 years or above. This decision came after a comprehensive data package that included longer-term follow-up for up to six months after the second dose of COMIRNATY® showed high efficacy and favorable safety profile. COMIRNATY is the first COVID-19 vaccine to be granted full approval by the FDA. Clinical trial registration #: NCT04900467
- On 20th August 2021, Zydus Cadila announced that Drugs Controller General of India (DCGI) has granted Emergency Use Authorization (EUA) for its plasmid deoxyribonucleic acid (DNA) vaccine, ZyCoV-D, for Covid-19. The EUA permits the use of the vaccine in adults as well as adolescents between the aged of 12 to 18 years. ZyCoV-D is a three-dose vaccine administered on day zero, day 28th and day 56th using PharmaJet®, a needle free applicator, which ensures painless intradermal vaccine delivery.
- On 18th August 2021, public health and medical experts from the U.S. Department of Health and Human Services (HHS) jointly released a statement on the plan for rolling out of COVID-19 booster shots to the American people. Prior to the administration, FDA will conduct independent evaluation and determination of the safety and effectiveness of a third dose of the Pfizer and Moderna mRNA vaccines and CDC's Advisory Committee on Immunization Practices (ACIP) will provide booster dose recommendations based on a thorough review of the evidence. It is anticipated that booster dose shots will start to be administered from 20th September 2021 to individuals who received a second dose of Pfizer and Moderna mRNA vaccines eight and above months before.

Therapeutics trials:

- On 25th August 2021, Emergent BioSolutions announced the initiation of a Phase 3 clinical trial, INSIGHT-012, to investigate its COVID-19 Human Immune Globulin Intravenous (COVID-HIG) plasma-derived therapy for treatment of COVID 19 patients with high risk of progression to severe disease. INSIGHT-012 which is a randomized controlled trial will assess whether giving people anti-coronavirus hyperimmune globulin at the onset of COVID-19 symptoms could potentially reduce the risk of more serious illness and death in high-risk outpatients including people aged 55 years and above and immunocompromised patients aged 18 years and above. The trial will enroll nearly 800 participants at sites in the US and other countries globally. Clinical trial registration #: NCT04910269
  On 24th August 2021, Brii Biosciences announced positive interim data from the phase 3 ACTIV-2 trial evaluating combination treatment of BRII-196 and BRII-198 in non-hospitalized COVID-19 patients. Results showed that monoclonal antibody combination therapy, BRII-196/BRII-198, reduced combined endpoint of hospitalization and death by 78% compared with placebo in 837 COVID-19 patients at high risk of clinical progression. Furthermore, drug-related serious adverse events (SAEs) or deaths were not reported in either of the arms in the trial. Clinical trial registration #:NCT04518410
- On 24th August 2021, EOM Pharmaceuticals announced that the first subjects have been dosed in the proof-of-concept Phase I/IIa R¹: RESCUE clinical trial of its peptide-nucleic acid solution immunomodulator , EOM613, in hospitalized Covid-19 patients with severe symptoms in Brazil. This open-label multicenter clinical study will recruit about 40 hospitalized COVID-19 patients at hospital sites in Brazil. It aims to assess safety, tolerability, and preliminary efficacy of EOM613 in non-ICU hospitalized patients and ICU hospitalized patients.
- On 20th August 2021, AstraZeneca reported positive results from the PROVENT Phase III clinical trial of its antibody combination, AZD7442, for prevention of Covid-19. Results showed that AZD7442, a combination of two long-acting antibodies (LAAB), reduced the risk of developing symptomatic COVID-19 by 77% compared to placebo. Furthermore, data showed that AZD7442 was well tolerated and adverse events were balanced between the placebo and AZD7442 groups. This randomized, double-blind, placebo-controlled, multi-center study enrolled 5,197 adults at 87 sites in the US, UK, Spain, France and Belgium. More than 75% of its participants had comorbidities. Clinical trial registration #: NCT04625725
- On 16th August 2021, Senhwa Biosciences announced that it has completed enrollment of a Phase 2 Investigator Initiated Trial (IIT) of its oral drug, Silmitasertib, for treatment of COVID-19 in the United States. This open-label, randomized, 2 arm parallel-group controlled, interventional study enrolled a total of 20 patients with moderate COVID-19 at 2 clinical sites within the United States. The trial aims to evaluate the safety, tolerability and pharmacokinetics of Silmitasertib in patients diagnosed with moderate COVID-19 and also seeks to compare time to clinical recovery and clinical benefit across the treatment groups. Silmitasertib is a first-in-class small molecule drug that targets Casein Kinase 2 (CK2) which is a key protein that triggers mechanisms vital for viral replication. Clinical trial registration #: NCT04663737
- On 15th August 2021, Enlivex Therapeutics Ltd reported that Israeli Ministry of Health has authorized the initiation of Phase IIb clinical trial of its universal, off-the-shelf cell therapy, Allocetra™ in severe and critical COVID-19 patients with acute respiratory distress syndrome (ARDS). This multi-center, placebo-controlled, randomized, blinded is expected to recruit up to 152 severe or critical COVID-19 patients in Israel and certain European countries. The trial will assess safety and efficacy of Allocetra™ when administered alongside standard of care treatment and also evaluation of long-COVID-19 symptoms. It will have two primary endpoints: ventilation-free survival and recovery for severe and critical patients. Clinical trial registration #: NCT04922957

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 21st to 27th August 2021.

Country	PHSM Trend	PHSM Change
Tier 4 (High Alert): Daily case incidence per 1M people/day ≥ 80 and/or positivity rate ≥ 12%		
Guinea-Bissau	↑	Officials in **Guinea-Bissau** extended the nationwide state of calamity by 15 days and implemented new domestic measures until 10 September 2021, including a nightly curfew, closure of religious institutions, and movement restrictions into and out of Bissau, Safim, and Prabis.
Mauritius	↓	**Mauritius** began its phased reopening to tourists, allowing fully-vaccinated travellers to enter the country starting 1 September 2021, but they must take a PCR test upon arrival and quarantine for 7 days. Unvaccinated travellers will be required to take a PCR test and quarantine for 14 days.
Morocco	→	**Morocco** extended the nationwide state of health emergency until 31 October 2021. Under current measures, a nightly curfew remains in place, and only vaccinated individuals are permitted to travel to and from tourist hubs including Casablanca and Marrakech.
Tunisia	↑	Officials in **Tunisia** updated requirements for incoming passengers. Travellers are required to present a negative PCR test within 72 hours of arrival, and unvaccinated travellers will be required to quarantine at a designated hotel for 10 days upon arrival.
Tier 3 (Moderate Alert): Daily case incidence per 1M people/day is 20 to <80 and/or positivity rate is 5% to <12%		
Zimbabwe	↓	Schools in **Zimbabwe** will reopen on Monday, 30 August 2021. Officials also announced that restaurants can reopen, but only to fully-vaccinated customers, and inter-city travel is permitted to resume.
Tier 2 (Low Alert): Daily case incidence per 1M people/day is 5 to <20 and/or positivity rate is 3% to 5%		
Algeria	↓	**Algeria** reopened beaches and places of leisure, the first measures loosened since the third wave began.
Uganda	↑	Travellers into **Uganda** will now be required to take a COVID-19 test upon arrival, regardless of vaccination status, as of 3 September 2021.
Tier 1 (Standard Precautions): Daily case incidence per 1M people/day is <5 and/or positivity rate is <3%		

Madagascar	→	**Madagascar** extended the nationwide state of health emergency for an additional 15 days. Individual protective measures such as wearing a face mask and social distancing must be adhered to in public, and public gatherings of more than 400 people indoors remain prohibited.

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

Contributors

In alphabetical order:

Alimi, Yewande; Dadji, Kwami Hoenoukpo; Hussein, Ally K; Loembé, Marguerite Massinga; Neema, Camara; Nshimirimana, Jean Claude; Onwuekwe, Ezinne; Sounga, Carine Sylvie; Tshangela, Akhona; Waya, Chimwemwe.

For any queries, kindly contact: Akhona Tshangela (AkhonaT@africa-union.org)