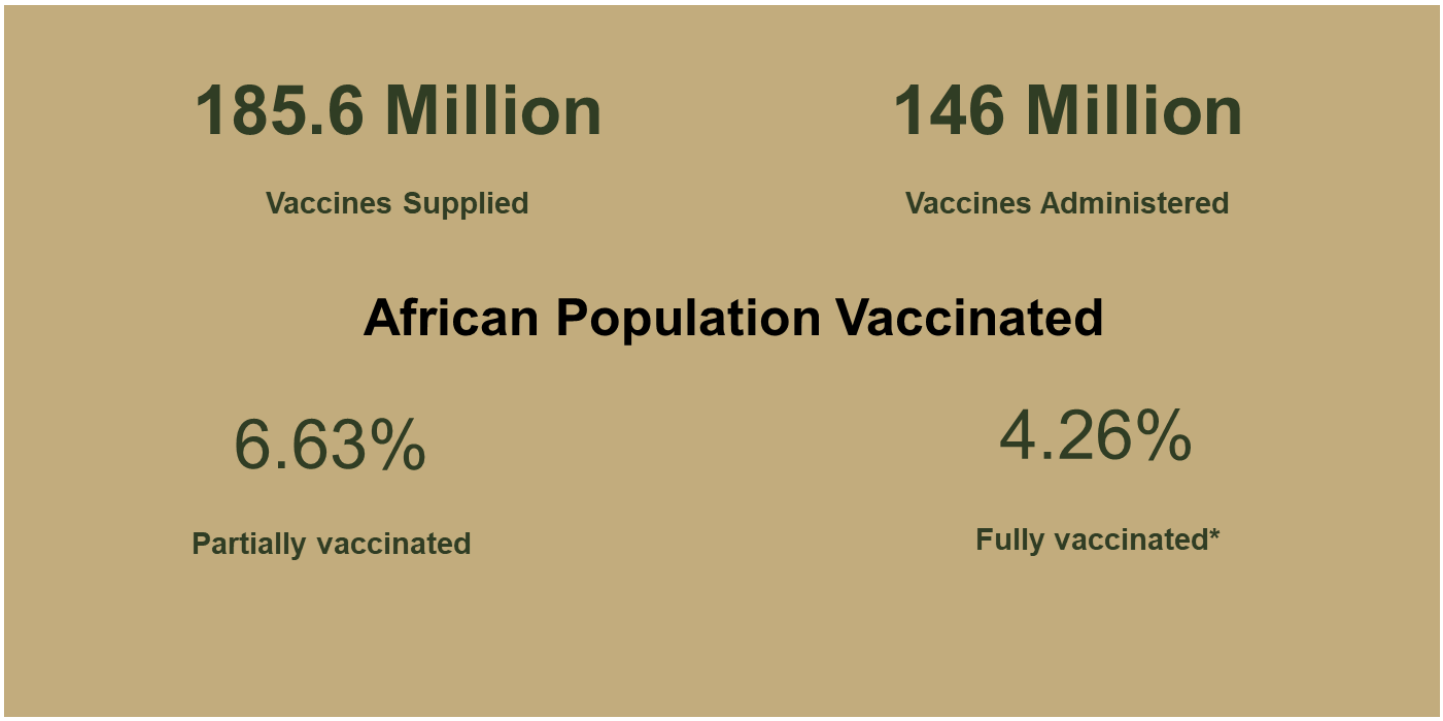
COVID-19 Scientific and Public Health Policy Update[1] – (28 September 2021)

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

A. Trending Topics

Status of Vaccines in Africa



*Received two doses/ one dose of Johnson & Johnson vaccine
https://africacdc.org/covid-19-vaccination/
Updated 28th September 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 187 countries worldwide; 40 Member States in Africa have reported this variant. https://africacdc.org/institutes/africa-pathogen-genomics-initiative/

Updated 28th September 2021

B. New guidelines and resources

Since 11th September 2021,

- Africa CDC has published new guidance and resources on:
  - African Union and the Africa CDC's Africa Regulatory Taskforce has endorsed the Emergency Use Authorization of Sinovac COVID-19 vaccine (Vero Cell [Inactivated]) – CoronaVac
  - African Union and the Africa CDC's Africa Regulatory Taskforce has endorsed the Emergency Use Authorization for COVID-19 Vaccine BIBP/ Sinopharm
- US CDC has published new guidance and resources on:
  - Operational considerations for adapting a contact tracing program to respond to the COVID-19 pandemic in non-US Settings
  - Interim guidelines for COVID-19 antibody testing
  - COVID-19 Vaccination Program operational guidance

- Strategies for optimizing the supply of N95 respirators
- Ending isolation and precautions for people with COVID-19: Interim Guidance
- Strategies for optimizing the supply of eye protection

- WHO has published new guidance and resources on:
  - Therapeutics and COVID-19: living guideline
  - Strengthening infection prevention and control in primary care
  - Frequently asked questions: COVID-19 vaccines and breastfeeding based on WHO interim recommendations
  - WHO competency framework: Building a response workforce to manage infodemics
- FDA has issued press releases on:
  - On 22nd September 2021, FDA authorizes booster dose of Pfizer-BioNTech COVID-19 vaccine for certain populations
  - Enforcement Policy for Face Masks, Barrier Face Coverings, Face Shields, Surgical Masks, and Respirators During the Coronavirus Disease (COVID-19) Public Health Emergency (Revised)
  - As of 17th September 2021, 410 tests and sample collection devices are authorized by the FDA under emergency use authorizations (EUAs)
- ECDC has issued new resources on:
  - Overview of the implementation of COVID-19 vaccination strategies and deployment plans in the EU/EEA
  - Protocol for a focused after-action review on evidence-based decision-making for selected COVID-19 response measures
- PHE has issued new guidance and press releases on:
  - COVID-19: provision of immunisation sessions for outbreaks in schools
  - JCVI issues updated advice on COVID-19 booster vaccination
  - COVID-19: infection prevention and control (IPC)
  - Middle East Respiratory Syndrome (MERS-CoV) risk assessment
  - Guidance for contacts of people with confirmed coronavirus (COVID-19) infection who do not live with the person
  - COVID-19: guidance for households with possible coronavirus infection

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 review create a framework for understanding SARS-COV-2 variants by describing fundamental aspects of SARS-CoV-2 evolution, the structure and function of the SARS-CoV-2 spike protein and the laboratory methods used to characterize spike variants. They then describe the biological properties and epidemiological characteristics of the variants and their associated mutations. Lastly, they describe the types of study required for the research, clinical and public health communities to respond to the new threat posed by emerging SARS-CoV-2 variants.
- This study offers a detailed structural and competitive landscape of key antibody binding sites on SARS-CoV-2 Spike. Their results can be used to predict and interpret effects of Variants of Concern (VOCs), and for strategic selection of durable therapeutics and cocktails against emerging variants.

- This review aimed to outline the plausibility of Suppressor of Cytokine Signalling (SOCS) protein inhibitors as a potential therapeutic regimen for COVID-19 patients. The authors also discuss the antagonists against SOCS protein to offer an overview on the previous 'successes' of SOCS protein inhibition in various viral infections that may portray possible clues for COVID-19 disease management.
- This study assessed the association of S-Adenosylmethionine (SAM) and S-Adenosylhomocysteine (SAH), indicators of global transmethylation, and severity of lung Injury in 56 COVID-19 patients admitted in Russia. The authors found that high plasma SAM levels and high methylation index were associated with the risk of lung injury in COVID-19 patients. Interleukin-6 (IL-6) levels were also associated with SAM. The association of SAM and SAH with IL-6 indicates an important role of transmethylation in the development of cytokine imbalance in COVID-19 cases. [*not peer reviewed*]
- This study investigated the immunomodulatory effects of COVID-19 convalescent plasma (CCP). The authors used an in vitro whole blood assay employing synthetic toll-like receptor (TLR) ligands and healthy donor leukocytes to test their hypothesis. All CCP samples were donated from healthy individuals at the Paul Ehrlich Institute, Germany. They report that CCP significantly decreased pro-inflammatory cytokines production triggered by different TLR ligands in healthy donors as compared to healthy control plasma. Their experiments reveal a potential novel, SARS-CoV-2-independent immunomodulatory activity of COVID-19 convalescent plasma, which may be beneficial for COVID-19 patients.

Vaccines

- This test-negative case–control study aimed to evaluate the effectiveness of mRNA vaccines in preventing COVID-19 among health care personnel. The study involved 1482 case participants and 3449 control participants across 25 U.S. states. The authors report the effectiveness for partial vaccination was 77.6% (95% CI, 70.9 to 82.7) with the BNT162b2 vaccine (Pfizer–BioNTech) and 88.9% (95% CI, 78.7 to 94.2) with the mRNA-1273 vaccine (Moderna); for complete vaccination, vaccine effectiveness was 88.8% (95% CI, 84.6 to 91.8) and 96.3% (95% CI, 91.3 to 98.4), respectively. Vaccine effectiveness was similar in subgroups defined according to age (<50 years or ≥50 years), race and ethnic group, presence of underlying conditions, and level of patient contact.
- This study examined the antibody responses of kidney transplant recipients who did not respond to 2 doses and received a third dose (100 µg) of the mRNA-1273 (Moderna) vaccine. The authors followed up 159 kidney transplant recipients at the Strasbourg University Hospital, France. They found that a third dose of mRNA-1273 vaccine induced a serologic response in 49% of kidney transplant recipients who did not respond after 2 doses. Patient receiving triple immunosuppression did not develop anti–SARS-CoV-2 antibodies even after the third dose.
- This interim analysis of an ongoing randomised, double-blinded, placebo-controlled, phase 3 clinical trial aimed to evaluate the efficacy of the measles-mumps-rubella (MMR) vaccine in preventing SARS-CoV-2 infection and severity of COVID-19 in health workers in Brazil. The authors report that MMR vaccine did not prevent SARS-CoV-2 infection, but the administration of at least one dose of the vaccine resulted in a significant reduction of 48% in symptomatic COVID-19 and of 76% in the need for treatment. When the participants used two doses, the reduction was 51% and 78%, respectively.[*not peer reviewed*]
- This retrospective study aimed to estimate the number of SARS-CoV-2 infections and COVID-19-related hospitalisations and deaths that have been averted via the nationwide vaccination campaign in Israel. The authors used national surveillance data routinely collected by the Ministry of Health from the first 112 days (Dec 20, 2020, up to April 10, 2021) of the vaccination campaign. They estimated that the campaign averted 158,665 (95% CI 144,640–172,690) SARS-CoV-2 infections, 24,597 (18,942–30,252) hospitalisations, 17,432 (12,770–22,094) severe or critical hospitalisations, and 5,532 (3,085–7,982) deaths. Without vaccination, Israel would have likely experienced approximately three times the number of hospitalisations and deaths compared with what actually occurred during its largest wave of SARS-CoV-2, which would have likely overwhelmed the health-care system.

- This case series of 22 patients with suspected allergic reactions to mRNA COVID-19 vaccines aimed to characterise the immunologic mechanisms underlying the allergic reactions in the United States. The patients received clinical skin prick testing (SPT) and basophil activation testing (BAT) to the whole vaccine and key components (i.e., polyethylene glycol [PEG] and polysorbate 80). The authors found that none of the patients exhibited immunoglobulin (Ig) E–mediated allergy to components via SPT. However, most had positive BAT results to PEG, and all had positive BAT results to their administered mRNA vaccine, with no patient sample having detectable PEG IgE. These findings suggest that non–IgE-mediated allergic reactions to PEG may be responsible for many documented cases of allergy to mRNA vaccines.
- This cohort study aimed to assess the association between baseline vaccine hesitancy and vaccine receipt at study follow-up and explored the validity of vaccine self-report. The study was conducted in the US among 4654 respondents. The authors found that COVID-19 vaccine hesitancy is not a stable trait precluding vaccination but, instead, is labile. Hesitancy decreased between late 2020 and early 2021, with nearly one-third of persons who were initially hesitant being vaccinated at follow-up and more than one-third transitioning from vaccine hesitant into vaccine willing. Self-reported vaccine receipt indicated substantial validity compared with the reference standard detection of anti-spike IgG among 1949 participants. Self-report had 98.2% positive predictive value, 97.3% negative predictive value, 94.8% sensitivity, and 99.1% specificity.
- This randomised, placebo-controlled, observer-blinded, phase 2–3 trial assessed the safety, efficacy, and immunogenicity of the BNT162b2 vaccine in adolescents and adults in the United States, Argentina, Brazil, South Africa, German and Turkey. The authors randomly assigned 44,165 participants 16 years of age or older and 2264 participants 12 to 15 years of age to receive two 30-µg doses, at 21 days apart, of BNT162b2 or placebo. They found that BNT162b2 continued to be safe and had an acceptable adverse-event profile. Vaccine efficacy against COVID-19 was 91.3% (95% CI, 89.0 to 93.2) through 6 months of follow-up. There was a gradual decline in vaccine efficacy. Vaccine efficacy of 86 to 100% was seen across countries and in populations with diverse ages, sexes, race or ethnic groups, and risk factors for COVID-19. Vaccine efficacy against severe disease was 96.7% (95% CI, 80.3 to 99.9). In South Africa, where the SARS-CoV-2 variant of concern B.1.351 (or beta) was predominant, a vaccine efficacy of 100% (95% CI, 53.5 to 100) was observed.
- This study used initial data from the Israeli Ministry of Health database to evaluate the rates of confirmed infection and severe illness among participants who were 60 years of age or older and who had received a third booster dose as compared with those who had received only two vaccine doses. The authors found that, at least 12 days after the booster dose, the rate of confirmed infection was lower in the booster group than in the non-booster group by a factor of 11.3 (95% CI, 10.4 to 12.3); the rate of severe illness was lower by a factor of 19.5 (95% CI, 12.9 to 29.5). In a secondary analysis, the rate of confirmed infection at least 12 days after vaccination was lower than the rate after 4 to 6 days by a factor of 5.4 (95% CI, 4.8 to 6.1).
- This phase I, adaptive, open, and monocentric clinical trial in Cuba, aimed to assess the safety and immune responses after application of a single dose of FINLAY-FR-1A vaccine (50 µg of the recombinant dimeric receptor binding domain) to 30 individuals with documented pre-existing SARS-CoV-2 natural immunity. There were no serious adverse events reported. Minor adverse events were found, the most common, local pain: 3 (10%) and redness: 2 (6.7%). The vaccine elicited a >21-fold increase in IgG anti-RBD antibodies 28 days after vaccination. The median of inhibitory antibody titres (94·0%) was three times greater than that of the COVID-19 convalescent panel. Virus neutralization titres higher than 1:160 were found in 24 (80%) participants. Their findings imply that a single dose of the FINLAY-FR-1A vaccine against SARS-CoV-2 is an efficient booster of pre-existing natural immunity, with excellent safety profile.
- This cohort study among 110 participants in Netherlands compared the SARS-CoV-2 Spike protein specific IgG antibody levels and neutralising antibody titres of sera before and after the first and second dose of BNT162b2 (Pfizer-BioNTech) mRNA vaccine between (1) participants infected within six months prior to vaccination, (2) previously infected participants infected earlier (over six months prior to vaccination) and (3) previously uninfected participants. The authors found that one dose of the BNT162b2 mRNA vaccine induces humoral immune responses in individuals previously infected with

SARS-CoV-2 exceeding those of uninfected individuals after two doses, whether infected occurred recently or over six months prior to vaccination. Delayed administration of the second vaccination dose for individuals with previous infection up to ten months, and likely longer, may constitute a more efficient vaccination strategy.

Diagnostics

- This study used a combination of the Nucleoprotein (NP), the Spike 1 (S1) and Spike 2 (S2) subunits, and the receptor binding domain (RBD) and N-terminal domain (NTD) of the Spike antigens from the Syrius-CoViDiag multiplex IgG assay, to follow the immune response to SARS-CoV-2 infection over a long time period and depending on disease severity. The authors used a panel of 209 sera collected from 61 patients up to 8 months after infection. They found that most patients develop an immune response against multiple viral epitope, but anti-S2 antibodies seemed to last longer. For all the tested IgGs, they found higher titres for hospitalized patients than for non-hospitalized ones. Moreover the combination of the five different IgG titres increased the correlation to the neutralizing antibody titres than if considered individually.[*not peer reviewed*]
- This study aimed to validate the Abbott Panbio COVID-19 rapid antigen test (RAT) among people attending the public test street in Sint Maarten, Dutch Caribbean. The authors used a RT-PCR Ct cut-off value of <33, they report that 119 out of 1,411 people (8.4%) tested positive for SARS-CoV-2. Most were asymptomatic (59%). The overall sensitivity and specificity of the RAT was 84% and 99.9% respectively. The sensitivity reduced to 67.6% among people without symptoms, regardless of whether they were in close contact with a known COVID-19 case. Sensitivity reduced considerably with a Ct cut-off value of <35. [*not peer reviewed*]

Care and Treatment

- This randomised, double-blind, placebo-controlled, phase 3 trial aimed to assess the efficacy and safety of subcutaneous REGEN-COV (Casirivimab and Imdevimab) in preventing SARS-CoV-2 infection among previously uninfected household contacts of infected persons and in treating recently infected asymptomatic persons. The trial was conducted at 112 sites in the United States, Romania, and Moldova among 2475 participants. The authors found that subcutaneous REGEN-COV prevented symptomatic COVID-19 and asymptomatic SARS-CoV-2 infection in previously uninfected household contacts of infected persons. REGEN-COV reduced the duration of symptomatic disease and the duration of a high viral load among the participants who became infected. REGEN-COV has potential use as long-term prophylaxis in persons at risk for SARS-CoV-2 infection.
- This prospective cohort study aimed to explore the impact of anticoagulation on COVID-19 related hospitalization and mortality among outpatients and inpatients. The study involved 6195 patients from 12 hospitals and 60 clinics in the US. The authors found that outpatients with COVID-19 who were on outpatient anticoagulation at the time of diagnosis experienced a 43% reduced risk of hospitalization. Failure to initiate anticoagulation upon hospitalization or maintaining outpatient anticoagulation in hospitalized COVID-19 patients was associated with increased mortality risk. They recommend further studies on anticoagulation therapy in COVID-19 patients to address critical questions including the type of anticoagulant, dosage, or duration of therapy.
- This study reports on the potent antiviral effect of the combination of Molnupiravir and Favipiravir in the SARS-CoV-2 hamster infection model. The authors found that, whereas suboptimal doses of either drug result respectively in ~1.2 $\log_{10}$ reduction in infectious virus titres in the lungs, the combination causes a >4.5 $\log_{10}$ reduction of such titres. When start of the combination treatment was delayed for 6 or 24 hours, a reduction of infectious titres in the lungs of respectively 3.1 and 2.4 $\log_{10}$ was achieved. Treatment of infected animals nearly completely prevented transmission to co-housed untreated sentinels. They also demonstrate that the potent antiviral efficacy in the combination group may be explained by an increased mutation rate of the viral genome as compared to the monotherapy treatment.

- This retrospective study aimed to determine the potential predictors for mortality in children hospitalised with SARS-CoV-2 infection. The authors compared demographic, clinical, laboratory and radiological parameters of 255 patients with different clinical outcomes at a tertiary care paediatric centre in New Delhi, India. They found that hypoxia at admission, involvement of three or more organ systems, presence of acute kidney injury, thrombocytopenia and raised levels of serum C-reactive protein were independently associated with increased odds of in-hospital mortality in children admitted with SARS-CoV-2 infection.
- This observational study aimed to investigate the therapeutic response of refractory COVID-19 or post-COVID-19 headache to indomethacin. The study involved 37 patients with and without migraine seeking help at a tertiary headache centre in Brazil. The authors prescribed Indomethacin at a dose of 50mg, twice a day, orally for 5 days. After treatment with indomethacin, 36 patients reported greater than 50% headache relief from the third day and 5 became asymptomatic on the fifth day. The authors recommend further studies on using indomethacin for the treatment of refractory COVID-19 headaches.

Epidemiology

- This single-centre, cross-sectional study aimed to describe the clinical characteristics and outcomes of patients with COVID-19 infection in Gabon, from March to June 2020. The study included 837 patients. The authors report that the mortality rate associated with COVID-19 was low (1.4%). About two thirds (63%) of the patients were asymptomatic, 33.7% had mild symptoms, and 31 (3.7%) had severe symptoms. Severity of disease and mortality were associated with advanced age and advanced stage of lung damage. Findings from this observational study provide preliminary data for use in future epidemiologic studies of COVID-19 in Gabon.
- This cross-sectional study aimed to evaluate the coinfection rate between SARS-CoV-2 and vector-borne diseases (VBD) in Luanda, Angola. The study involved 105 participants tested for SARS-CoV-2, malaria, and dengue in April 2021. The participants tested positive for SARS-CoV-2 (3.80%), malaria (13.3%), and dengue (27.6%). The overall co-infection rate between SARS-CoV-2 and VBD was 11.4%. Their findings could indicate the need to integrate the screening for VBD in the SARS-CoV-2 testing algorithm and the adjustment of treatment protocols.
- This systematic review aimed to summarise the descriptive epidemiology and clinical characteristics of multisystem inflammatory syndrome in adults (MIS-A). The study included 221 patients worldwide with MIS-A reported in the literature and to the US Centers for Disease Control and Prevention. The syndrome presented approximately 4 weeks after acute COVID-19 with hyper inflammation and extra pulmonary multiorgan involvement that may be difficult to discern from acute biphasic COVID-19 and post-acute sequelae of SARS-CoV-2 infection. Most patients presented with fever [96%], hypotension [60%], cardiac dysfunction [54%], shortness of breath [52%], and/or diarrhoea [52%].
- This pilot quality improvement program in Nebraska, US, aimed to characterize SARS-CoV-2 infections in staff and students in an urban public-school setting and evaluate test-based strategies to support ongoing risk assessment and mitigation for kindergarten through 12th grade in-person learning. The authors found that weekly screening of asymptomatic staff and students by saliva polymerase chain reaction testing was associated with increased SARS-CoV-2 case detection, exceeding infection rates reported at the county level. SARS-CoV-2 was detected in school wastewater samples each week as well as air and surface samples from choir classrooms.
- The authors in this modelling study developed PyR_0, a hierarchical Bayesian multinomial logistic regression model that infers relative transmissibility of all viral lineages across geographic regions, detects lineages increasing in prevalence, and identifies mutations relevant to transmissibility. They applied the model to all publicly available SARS-CoV-2 genomes, and identified numerous substitutions that increase transmissibility, including previously identified spike mutations and many non-spike mutations within the nucleocapsid and non-structural proteins. [*not peer reviewed*]

Infection Prevention and Control

- The authors in this study aimed to develop a simple, inexpensive and ecological method for decontamination of disposable filtering face pieces (FFPs) that preserves filtration efficiency and material integrity. They performed experiments to decontaminate FFPs by submersion in a solution of 6% acetic acid and 6% hydrogen peroxide (6%AA/6%HP solution) over 30 minutes. This resulted in the complete elimination of SARS-CoV-2, E. faecium and physiological nasopharyngeal flora. Material characterization post-treatment showed neither critical material degradation, loss of fit or reduction of filtration efficiency. Electron microscopy revealed no damage to the fibres, and the rubber bands' elasticity was not affected by the decontamination procedure.
- This multicentre, non-blinded *in-situ* simulation study in South Africa aimed to assess the fit, seal, and clinical usability of an adapted snorkel mask. The masks provide full-face protection for healthcare workers, particularly during aerosol-generating procedures. The fit-tested modified full-face snorkel mask may offer benefit as a substitute for N95 respirators and face shields. The authors emphasize on selecting the correct mask based on size, fit testing, and quality of the three-dimensional (3D) printed parts & respiratory filter used.

Non-pharmaceutical interventions, social distancing

- This study compared the bacterial load and microbiome composition on certified disposable surgical masks and self-made cotton masks, to evaluate some risks for bacterial cross-contamination. Cotton and surgical masks were found to contain on average 1.46×10^5 CFU/mask and 1.32×10^4 CFU/mask, respectively. Bacillus, Staphylococcus, and Acinetobacter spp. were mostly cultured from the masks and 43% of these isolates were resistant to ampicillin or erythromycin. The authors recommend that face masks should be properly disposed of or sterilized after intensive use. Clear guidelines for the general population are crucial to reduce the bacteria-related biosafety risk of face masks, and measures such as physical distancing and increased ventilation should not be neglected when promoting face mask use.
- This modelling study aimed to estimate the impact of community face mask use, at varying levels of mask uptake and mask effectiveness during the roll out of vaccination in New York City. The authors report that a pre-emptive, early mandate for masks is more effective than late mask use, but even late mask mandates will reduce cases and deaths by over 20%. The epidemic curve is suppressed by at least 50% of people wearing a mask from the start of the outbreak but surges when mask wearing drops to 30% or less. With a slow roll out of vaccines over five months at uptake levels of 20–70%, non-pharmaceutical interventions use will still be needed and has a greater impact on epidemic control.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 23rd September 2021, Novavax and its partner, Serum Institute of India (SII) announced that they have filed a regulatory submission to the World Health Organization (WHO) for emergency use listing (EUL) of its Novavax' recombinant nanoparticle protein-based COVID-19 vaccine candidate with Matrix-M™ adjuvant. In addition to the submission for WHO EUL, the two companies completed the submission of modules required by regulatory agencies in India, Indonesia and Philippines for initiation of review of the vaccine, including preclinical, clinical, and chemistry, manufacturing and controls (CMC) data. The WHO grant of EUL to the vaccine is required before the company starts to export vaccines to numerous countries participating in the COVAX Facility.
- On 22nd September 2021, Clover Biopharmaceuticals, Ltd and the Coalition for Epidemic Preparedness Innovations (CEPI) announced that Clover's adjuvanted protein-based COVID-19 vaccine candidate, SCB-2019 (CpG 1018/Alum) had achieved a 67% vaccine efficacy against COVID-19 caused by SARS CoV-2 lineage or variants. According to data from SPECTRA, a global pivotal Phase 2/3 clinical trial, SCB-2019 (CpG 1018/Alum) demonstrated a 79% overall efficacy against Delta variant, 92% against

Gamma variant and 59% against Mu variant. This 1 :1 randomized, double-blinded, placebo-controlled Phase 2/3 SPECTRA clinical trial was conducted at 31 sites in five countries including Philippines, Brazil, Colombia, **South Africa** and Belgium. The aim of the study was to evaluate the efficacy, safety and immunogenicity of SCB-2019 (CpG 1018/Alum) compared to placebo. The trial enrolled over 30,000 adult and elderly (≥18 years of age) subjects. Clinical trial registration #: NCT04672395

- On 22nd September 2021, the U.S. Food and Drug Administration granted emergency use authorization (EUA) for a single booster dose of Pfizer-BioNTech COVID-19 vaccine to be administered to elderly ≥ 65 years of age at least six months after completion of the primary series. The booster dose is also intended for people aged 18 to 64 years at increased risk of severe Covid-19, as well as for people whose regular institutional or occupational exposure to SARS-CoV-2 places them at an increased risk of serious complications of the infection. This decision comes after critical analysis of submitted scientific clinical trial data that were conducted by the manufacturers and FDA to assess the safety, tolerability and immunogenicity of the booster. It was determined that BioNTech COVID-19 Vaccine may be effective in preventing COVID-19 and that the known and potential benefits of a booster dose outweigh the known and potential risks in the populations targeted for use.
- On 21st September 2021, Johnson & Johnson reported new data confirming the strong and long-lasting protection of its COVID-19 vaccine against COVID-19-related hospitalizations and deaths. According to data from effectiveness studies reported in the U.S so far, stable vaccine effectiveness of 79% (95% CI, 77%-80%) for COVID-19-related infections and 81% (95% CI, 79%-84%) for COVID-19-related hospitalizations were observed when the Delta variant became dominant in the U.S. The study was conducted from March to late July 2021 and enrolled 390,000 subjects who received J&J COVID-19 vaccine and were matched with1.52 million unvaccinated people based on age, sex, time, zip code, comorbidities and predictors for COVID-19 infection severity. The company has submitted the data to the U.S. Food and Drug Administration (FDA) and is expected to submit to the World Health Organization (WHO) and National Immunization Technical Advisory Groups (NITAGs) worldwide to inform on local vaccine administration strategies.
- On 20th September 2021, Pfizer and BioNTech announced the positive top-line results from a Phase 2/3 trial which showed their COVID 19 mRNA vaccine, Comirnaty, have favorable safety profile and robust neutralizing antibody responses in children 5 to 11 years of age. The results were based on data obtained from 2,268 participants between 5 to 11 years of age who had received 10 µg doses administered 21 days apart. Geometric mean titer (GMT) for SARS-CoV-2–neutralizing antibody was 1,197.6 (95% CI, 1106.1-1296.6] demonstrating strong immune response after the second dose of the vaccine. The vaccine was well tolerated, with side effects generally comparable to those observed in participants 16 to 25 years of age. Pfizer and BioNTech plan to share these data with the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA) and other regulators as soon as possible. Clinical trial registration # : NCT04816643
- On 17th September 2021, researchers running the University of Oxford-led Com-COV programme announced the launch of a new study to assess mixed Covid-19 vaccine dose schedules in adolescents aged 12 to 16 years in the United Kingdom. The trial will test Pfizer-BioNTech, Novavax and Moderna Covid-19 vaccines as combination regimens in a minimum of 360 adolescents. Participants immunized with first dose of Pfizer-BioNtech will receive either second full dose Pfizer-BioNtech, half dose Pfizer-BioNtech, half dose Moderna or full dose Novavax at an eight-week interval. This single-blind, randomised, phase II multi-centre study aims to determine reactogenicity and immunogenicity of heterologous prime/boost COVID-19 vaccine schedules in adolescents. EudraCT Number: 2021-004267-27
- On 16th September 2021, Moderna announced that Health Canada has approved the New Drug Submission for its mRNA vaccine, SPIKEVAX to prevent COVID-19 disease in individuals 12 years of age and older. The decision was based on the positive results from Phase 3 COVE study of 30,000 participants from the United States. Data showed that the vaccine had a 93% efficacy which remained durable six months after administration of the second dose. In addition, the safety profile observed on extended safety follow-up was consistent with the Phase 3 COVE study primary results.

- On 15th September 2021, the Russian Direct Investment Fund announced positive data indicating a 97.2% efficacy of sputnik V vaccine against coronavirus during the vaccination campaign in Belarus. The efficacy of Sputnik V was measured based on data from > 860,000 peoples who were vaccinated between January and July 2021. The data from the Ministry of Health further confirmed safety of sputnik V vaccine after reports showed no deaths nor severe adverse events were associated with sputnik V vaccination.
- On 14th September 2021, City of Hope reported that it has started enrolment of participants into phase II clinical trial of its Covid-19 vaccine candidate, COH04S1, in immunocompromised people on immunosuppressive therapy. This multi-centre, observer-blinded, randomized phase II study aims to evaluate the biological activity of COH04S1 compared to SARS-CoV-2 vaccines with emergency use authorization (EUA) in haematology patients who have received cellular therapy (HCT or CAR-T). The trial will involve 240 blood cancer patients who are immunocompromised and received a bone marrow transplant or chimeric antigen receptor (CAR) T treatment in the United States. Clinical trial registration #: NCT04977024

Therapeutics trials:

- On 21st September 2021, Eiger Biopharmaceuticals announced that the Data Safety Monitoring Board (DSMB) recommended the investigators to continue enrolling subjects in the Peginterferon Lambda arm of the Phase III TOGETHER platform clinical trial in Covid-19 outpatients. Peginterferon Lambda is a well-characterized, late-stage, first-in-class, type III interferon (IFN) that stimulates immune responses that are critical for the development of host protection during viral infections. The multi-center, investigator-sponsored, randomized, placebo-controlled adaptive platform phase 3 TOGETHER study aims to evaluate therapeutics in newly diagnosed, high-risk, non-hospitalized patients with COVID-19. The trial will recruit up to 800 outpatients who are at increased risk for COVID progression at twelve sites in Brazil. Clinical trial registration #: NCT04967430
- On 17th September 2021, Appili Therapeutics reported that it has completed patient enrolment in the viral shedding sub-study portion of its Phase 3 PRESECO which is assessing vigan/Reeqonus (favipiravir), broad-spectrum antiviral oral tablet, as a potential therapy for Covid-19 in the United States. The aim of the study is to evaluate the safety and efficacy of favipiravir in the early treatment of mild-to-moderate adults infected with COVID-19 including recent and emerging variants. The sub-study has enrolled over 550 Covid-19 patients with mild-to-moderate symptoms in the outpatient setting in the United States. The trial is also recruiting participants at multiple clinical trial sites in Brazil and Mexico. Clinical trial registration #: NCT04600895
- On 16th September 2021, Biophytis SA announced that the Data Monitoring Committee (DMC) recommended the continuation of Phase 2/3 COVA clinical trial of its oral antiviral, Sarconeos (BIO101), without any protocol amendments. This came following promising interim efficacy data in the second interim analysis (IA2), which was based on 155 hospitalised Covid-19 patients with respiratory failure. This global, multicentric, double-blind, placebo-controlled, group-sequential, and adaptive design two-part Phase 2-3 COVA study aims to assess Sarconeos (BIO101) in patients aged ≥45 years and hospitalized with severe respiratory manifestations of COVID-19. The trial anticipates to recruit up to 465 subjects from six clinical centers opened in the USA, Brasil, France and Belgium. Clinical trial registration #: NCT04472728
- On 15th September 2021, Glenmark Pharmaceuticals announced the successful completion of its Post Marketing Surveillance (PMS) study on its oral antiviral drug, Favipiravir (FabiFlu), for the treatment COVID-19 patients in India. The prospective, open label, multicentre, single arm PMS study evaluated the safety and efficacy of Favipiravir in 1083 mild to moderate COVID-19 patients. The study began in July 2020 and included participants (mean age of 40 years and 60% of men). According to the PMS data, no new safety signals or concerns were observed and already-known side effects such as weakness, gastritis, diarrhoea, vomiting were found to be mild in nature. The time for fever resolution was 4 days, while time for clinical cure was 7 days.

- On 14th September 2021, RedHill Biopharma announced that the preliminary top-line data from the universal Phase 2/3 study of its drug, opaganib, failed to meet its primary endpoint. Analysis of the study efficacy endpoints did show trends in favour of the opaganib arm across multiple endpoints, including the primary endpoint, despite not achieving statistical significance. However, good tolerability and balanced adverse events between the study arms were observed. The multi-center, randomized, double-blind, parallel-arm, placebo-controlled Phase 2/3 study enrolled 475 subjects with severe COVID-19 who were hospitalized and treated with supplemental oxygen. Clinical trial registration #: NCT04467840
- On 13th September 2021, RedHill Biopharma Ltd announced that South African Health Products Regulatory Authority (SAHPRA) has approved phase 2/3 clinical trial of its new oral drug candidate, RHB-107 to treat non-hospitalised patients with symptomatic Covid-19 in **South Africa**. This 2-part, multicenter, randomized, double-blind, placebo-controlled, parallel-group study aims to evaluate the safety and efficacy of RHB-107. Time to sustained recovery from illness will be evaluated as the primary endpoint. The trial is currently being conducted in the United States with the expansion of trial centres underway to speed up subject enrolment. Clinical trial registration #: NCT04723537

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 18th to 24th September 2021.

Country	PHSM Trend	PHSM Change
Tier 4 (High Alert): Daily case incidence per 1M people/day ≥ 80 and/or positivity rate ≥ 12%		
Lesotho	↓	Lesotho partially eased nationwide COVID-19 restrictions, moving to Level Purple. Under this level, the nightly curfew has been reduced, capacity limitations on social gatherings were increased, and sports are permitted to resume with no spectators, among other measures.
Somalia	↑	Somalia tightened restrictions for travellers amid rising cases. All incoming passengers (except children under 12) must present a negative COVID-19 test taken within 72 hours of departure. Travellers who have been in a country designated high-risk must quarantine for 14 days upon arrival.
Tunisia	↓	Officials in Tunisia are lifting the nightly curfew in all regions as of 25 September 2021.
Tier 3 (Moderate Alert): Daily case incidence per 1M people/day is 20 to <80 and/or positivity rate is 5% to <12%		

Equatorial Guinea	↑	Several measures were implemented in Equatorial Guinea amid rising cases. A state of alarm was declared, the nationwide curfew was lengthened by 6 hours, travel between regions is restricted, and public transport must operate at reduced capacity.
Eswatini	↓	Eswatini moved to Adjusted Risk Level 2. Under the new directive, the nightly curfew was shortened and business hours were expanded.
Kenya	→	Kenya maintained some COVID-19 measures due to a spike in cases. The nightly curfew will remain in effect until 19 October 2021, public gatherings remain suspended, and religious services remain restricted.
Rwanda	↓/↑	Officials in Rwanda announced the reopening of bars after 18 months of COVID-related closures. The nightly curfew in Kigali was also reduced by one hour, while the curfew in high-incidence areas (including Gicumbi and Ngoma) has been tightened.
Tier 2 (Low Alert): Daily case incidence per 1M people/day is 5 to <20 and/or positivity rate is 3% to 5%		
Zimbabwe	↑	The level 2 lockdown in Zimbabwe was extended for an additional two weeks. Measures include a nightly curfew, restrictions on nonessential businesses, and capacity limits on social gatherings.
Tier 1 (Standard Precautions): Daily case incidence per 1M people/day is <5 and/or positivity rate is <3%		
Tier 0 (No Data Available)		
Uganda	↓	Additional COVID-19 restrictions were loosened in Uganda. Universities and post-secondary institutions were permitted to reopen on 1 November, places of worship can reopen at reduced capacity, and some social events, including funerals and weddings, are permitted to resume with a maximum of 200 people.

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

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