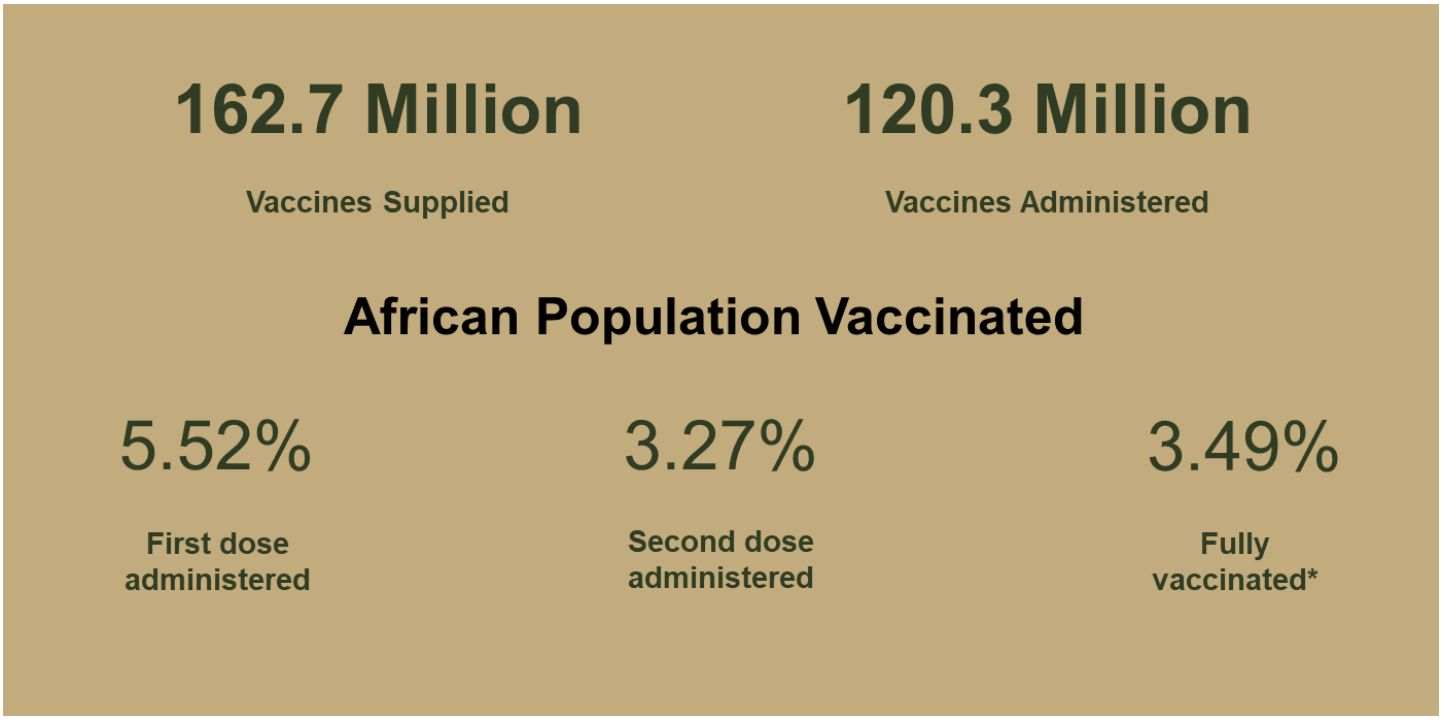
COVID-19 Scientific and Public Health Policy Update[1] – (14 September 2021)

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

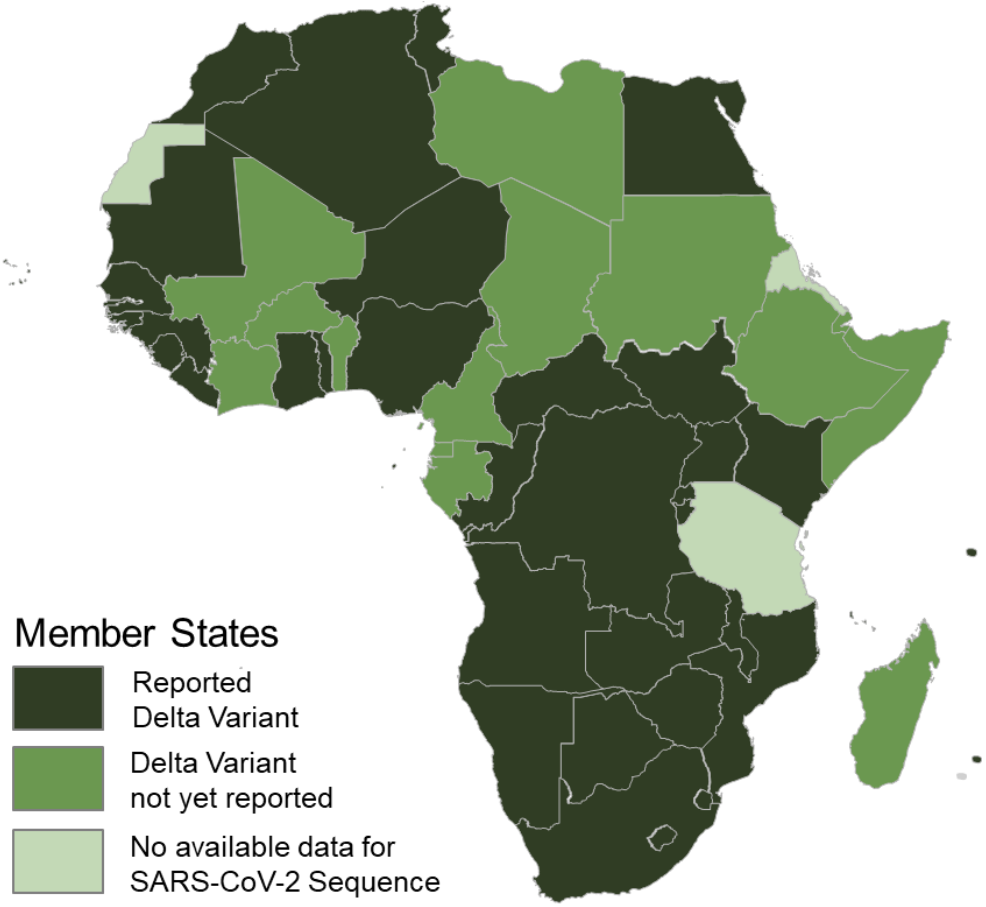


*Received two doses/ one dose of Johnson & Johnson vaccine
https://africacdc.org/covid-19-vaccination/
Updated 14th September 2021

Variants of Concern

- The Delta variant (B.1.617.2), first reported in India, has spread to more than 174 countries worldwide; 36 Member States in Africa have reported this variant. https://africacdc.org/institutes/africa-pathogen-genomics-initiative/

[1] This update compiled for use by African Union Member States and is developed collaboratively by the African Union-Africa CDC and World Health Organization - Regional Office for Africa. **This is a preliminary summary of information and not considered policy, guidance, or final conclusions of the African Union- Africa CDC or WHO/AFRO**.



Updated 9th September 2021

B. New guidelines and resources

Since 28th August 2021,

- Africa CDC has published new guidance and resources on:
  - Addressing Market Failures: The Role of CEPI in Bridging the Innovation Gap to Prevent the Next Pandemic
  - Interim operational guidance on SARS-CoV-2 genomic surveillance in Africa: An updated guide
  - Report: Cross Country Learning on Community Health System Integration and Financing

- US CDC has published new guidance and resources on:
  - Using Antibody Tests for COVID-19
  - Interim Infection Prevention and Control Recommendations for Healthcare Personnel During the Coronavirus Disease 2019 (COVID-19) Pandemic
  - Interim Guidance for Managing Healthcare Personnel with SARS-CoV-2 Infection or Exposure to SARS-CoV-2
  - Interim Guidance for Antigen Testing for SARS-CoV-2
  - Operational Considerations for Routine Immunisation Services during the COVID-19 pandemic in non-US Settings Focusing on Low- and Middle-Income Countries

- WHO has published new guidance and resources on:
  - How to manage COVID-19 vaccines without VVM at vaccination service points?
  - COVID-19 immunisation in refugees and migrants: principles and key considerations: interim guidance

- FDA has issued press releases on:
  - FDA Will Follow The Science On COVID-19 Vaccines For Young Children
  - FDA approved an abbreviated new drug application for dexmedetomidine injection USP, 200 mcg/2 mL
  - FDA made changes to the authorized use of the monoclonal antibodies bamlanivimab and etesevimab, administered together
  - FDA revised the guidance Development of Abbreviated New Drug Applications During the COVID-19 Pandemic – Questions and Answers
  - As of 10th September 2021, 409 tests and sample collection devices are authorized by the FDA under emergency use authorizations (EUAs)

- ECDC has issued new resources on:
  - Interim public health considerations for the provision of additional COVID-19 vaccine doses
  - Data collection on COVID-19 outbreaks in closed settings with a completed vaccination programme: long-term care facilities, version 2.0

- PHE has issued new guidance and press releases on:
  - COVID-19: infection prevention and control (IPC)
  - COVID-19 vaccination: a guide for eligible children and young people aged 16 to 17
  - Information for children and young people on what to expect after COVID-19 vaccination
  - COVID-19 vaccination for at-risk children and young people aged 12 to 15 (simple text)
  - Preventing and controlling outbreaks of COVID-19 in prisons and places of detention

The full list of latest guidance and resources from WHO and other public health institutions can be found in this link.

C. Scientific updates

Basic Science

- This cohort study aimed to evaluate the association between human leukocyte antigen alleles (HLA) and the severity of COVID-19. The authors analysed HLAs in 435 individuals from Germany, Spain, Switzerland and the United States. They found a potential association of HLA-C*04:01 with severe clinical course of COVID-19. Carriers of HLA-C*04:01 had twice the risk of intubation when infected with SARS-CoV-2. Their findings were corroborated by independent results from prior genome-wide association studies (GWAS). Their findings suggest that HLA class I alleles have a relevant role in immune defense against SARS-CoV-2.
- This study presents findings from a COVID-19/HIV co-infected decedent from Singapore who exhibited a longer survival time of 46 days compared to 3 others with an average of 30 days. The authors identified unique transcriptomic profiles, especially in the liver and kidney. The decedent exhibited a reduction of T-cells and elevation of macrophages only in the non-pulmonary tissues and no difference in the abundance of natural killer cells and other immune cell types across tissue types. Their findings suggest that HIV-mediated immunosuppression may lower the risk of COVID-19 disease progression. They recommend close monitoring of the immune status of myeloid cells in other organs such as the liver and further research on the COVID-19–HIV relationship to develop optimal treatment strategies.

- This study utilised the Friend retrovirus mouse model to show the requirement of nutrients and metabolism for the antiviral activity of Natural Killer (NK) cells. The experiments were conducted in Ireland. NK cells were found to reprogramme their metabolism by increasing their nutrient uptake, glycolysis and mitochondrial machinery after acute virus infection. The antiviral functions of NK cells strongly depend on sufficient levels of iron. This new understanding of the metabolism of NK cells in the acute phase of infection is essential to facilitate the development of novel metabolism-targeted approaches for treating infectious diseases including HIV and SARS-CoV-2.
- The authors in this study, conducted in the UK, report a proteomic screen for cellular factors that interact with the cytoplasmic tail of the spike (S) protein. Their findings confirm interactions with the COPI and COPII vesicle coats, ERM family actin regulators, and the WIPI3 autophagy component. S leaks to the surface where it accumulates and can direct the formation of multinucleate syncytia. The trafficking signals in the tail of S indicate that syncytia play a role in the SARS-CoV-2 lifecycle. They recommend further studies to investigate the importance of the intracellular location of S for both SARS-CoV-2 infection and vaccine design.

Vaccines

- This case-control study aimed to assess the effectiveness of Gam-COVID-Vac against lung injury and referral to hospital in St. Petersburg, Russia. The study included 13,893 patients. The authors report the adjusted vaccine effectiveness (VE) against referral to hospital was 81% for complete vaccination. The VE against referral to hospital was more pronounced in women compared to men. Vaccine protective effect increased with increasing lung injury categories. [*not peer reviewed*]
- This retrospective cohort study aimed to investigate the association between the rollout of the first component (rAd26) of Gam-COVID-Vac and PCR-positive tests, hospitalisations and deaths in Buenos Aires, Argentina. Their findings show that Gam-COVID-Vac prevents 78.6% of laboratory-confirmed SARS-CoV-2 infections, 87.6% of hospitalisations and 84.8% of deaths. The effectiveness was comparable across age subgroups.
- This prospective cohort study among 1647 health care workers in Belgium compared the humoral immune responses between those who received 2 doses of mRNA-1273 and BNT162b2. Authors report a significantly higher humoral immunogenicity of the SARS-CoV-2 mRNA-1273 vaccine compared with the BNT162b2 vaccine, in infected as well as uninfected participants, and across age categories.
- This prospective cohort study aimed to describe the assessment and immunisation of 429 highly allergic individuals with the BNT162b2 vaccine in Israel. The authors used an algorithm to define them from a cohort of 8102 individuals with an allergy history. The identified individuals received immunisation under medical supervision. Majority (98%) of the highly allergic individuals had no allergic reaction, 6 (1%) had mild allergic responses, and 3 (0.7%) had anaphylactic reactions. Their results suggests that most patients with a history of allergic diseases can be safely immunised by using an algorithm. They recommend further studies to define more specific risk factors for allergic reactions to the BNT162b2 vaccine.
- This case-control study aimed to assess the association between exposure characteristics and infection risk among vaccinated and non-vaccinated health care workers (HCWs) in Israel. The study involved a total of 171 HCWs. The authors found that exposure to SARS-CoV-2–positive household members was a risk factor associated with infection among vaccinated HCWs. Their findings suggest reconsideration of quarantining vaccinated people who have had significant exposure to household members who are positive for SARS-CoV-2 infection.
- This case series aimed to describe ocular adverse events that occur soon after receiving an inactivated COVID-19 vaccination (Sinopharm). The study was conducted in a tertiary referral centre in Abu Dhabi, UAE. Seven patients presented to the facility 5.2 days after administration of the vaccine with mild, reversible ocular adverse events, both in the anterior and posterior segment. A causal relationship cannot be established from this case series.

- This cohort study aimed to evaluate the SARS-CoV-2 antibody response in patients undergoing chronic haemodialysis following 1 vs 2 doses of BNT162b2 COVID-19 vaccination compared with health care workers serving as controls and convalescent serum. The study involved 142 patients receiving haemodialysis. The authors found poor immunogenicity 28 days following a single dose of BNT162b2 vaccine in the haemodialysis population. Their findings support the adherence to recommended vaccination schedules and avoiding delay of the second dose in these at-risk individuals.
- This interim analysis aimed to monitor 23 serious outcomes weekly, using comprehensive health records on a diverse population in the US. The authors analysed safety surveillance data from 6.2 million persons who received 11.8 million doses of an mRNA vaccine. They found that event rates for 23 serious health outcomes were not significantly higher for individuals 1 to 21 days after vaccination compared with similar individuals at 22 to 42 days after vaccination.
- This retrospective cohort study aimed to assess the safety of BNT162b2 in previously diagnosed cases of Guillian-Barré Syndrome (GBS) in Israel. The study included 702 patients. The authors report that only 1 patient needed short medical care for relapse of previous syndrome, which represents a minimal risk.
- This cohort study aimed to investigate the serological responses after a single dose of a SARS-CoV-2 vaccine among patients with inflammatory bowel disease treated with infliximab. The authors report that infliximab is associated with attenuated immunogenicity to a single dose of the BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines. Vaccination after SARS-CoV-2 infection, or a second dose of vaccine, led to seroconversion in most patients. Delayed second dosing should be avoided in patients treated with infliximab.
- This survey aimed to assess levels and predictors of self-reported intention to vaccinate against COVID-19 and identify key groups with low intention to vaccinate at the start of the vaccine rollout in Canada. A total of 14,621 participants completed the online survey form. The authors identified population groups with greater and lesser intention to vaccinate, the differences were observed by age, education, ethnicity, and provincial residence. As the vaccination efforts continue, policymakers may use this information to focus outreach, education, and other efforts.

Diagnostics

- This study compared the accuracy of a rapid antigen detection test using exhaled breath condensate by a modified Inflammacheck® device with the standard RT-PCR to diagnose SARS-CoV-2 infection. A total of 105 individuals were included, with the RT-PCR being positive in 13 (12.4%). The agreement between the two methods was 98.1%. The overall sensitivity and specificity of the Inflammacheck® were 92.3% and 98.9%, respectively. The PPV was 92.3% and NPV was 98.9%, with an overall accuracy of 98.1%. The device may be used for routine practice in different healthcare settings.
- The authors in this in silico study developed a support vector machine (SVM) method for the classification of patients with COVID-19 and patients with other pneumonias via a radiomics framework. Their final model showed good discrimination on the independent validation cohort, with an accuracy of 89.83%, sensitivity of 94.22%, specificity of 85.44%, and AUC of 0.940. Their results proved that the radiomics features in CT chest images were highly distinguishable, and that the SVM model could effectively identify and diagnose patients with COVID-19 and other pneumonias.

Care and Treatment

- This open-label, randomised controlled trial aimed to assess the efficacy of convalescent plasma in adults with COVID-19 receiving oxygen within 12 days of respiratory symptom onset. The trial involved 940 patients allocated 2:1 to 500 ml of convalescent plasma or standard of care. The authors found that convalescent plasma did not reduce the risk of intubation or death at 30 days in hospitalized patients with COVID-19. Moreover, transfusion of convalescent plasma with unfavourable antibody profiles could be associated with worse clinical outcomes compared to standard care.
- This prospective cohort study aimed to evaluate the proportions of elevated liver enzymes at hospital admission and their association with severe COVID-19 in 217 patients from the University Hospital in Munich. The authors report that 58% of patients had liver function test (LFT) abnormalities at the time

of hospital admission. They found a significant correlation of elevation of baseline LFT, including gamma-glutamyltransferase (GGT), as well as hypoalbuminaemia with more severe courses of SARS-CoV-2 infections.

- This retrospective cohort study aimed to assess the association of vitamin D levels and COVID-19 mortality risk. The study involved 1226 patients from 2 hospitals in the UK. The authors found no difference in the mortality in people with vitamin D deficiency compared with those with normal vitamin D levels after adjusting for comorbidities. The most vulnerable group was one with multiple comorbidities such as ischaemic heart disease, hypertension, chronic obstructive pulmonary disease, interstitial lung diseases, asthma, alcoholic liver disease, chronic liver diseases, dementia, frailty, current smoker, ex-smoker, diabetes mellitus type 1 and type 2.
- This cohort study aimed to investigate the association of diet quality with risk and severity of COVID-19 and its interaction with socioeconomic deprivation. The study utilised data from 592,571 participants of the smartphone-based COVID-19 symptom study in the UK and USA. The authors found that a diet characterised by healthy plant-based foods was associated with lower risk and severity of COVID-19. This association may be particularly evident among individuals living in areas with higher socioeconomic deprivation.
- This multicentre, retrospective, and observational study aimed to explore whether uric acid (UA) can independently predict the prognosis of severe patients with COVID-19 and whether it can be used as an index to evaluate the degree of the disease. The study included 540 patients from 4 hospitals in Wuhan. The authors found that the lowest concentration of UA during hospitalisation can be used as a prognostic indicator and a marker of disease severity in severe patients with COVID-19.
- This in silico study investigated the efficacy of Anthraquinolone (AQ) and Quinolizine derivatives (QZ) as inhibitors of SARS-CoV-2 main protease (M^{pro}). Prioritisation of cavity atoms obtained through pharmacophore mapping and other physicochemical descriptors of the derivatives helped the authors to map important chemical features for ligand binding interaction and also for synergistic studies with molecular docking. Their results were supported through simulation trajectories. They recommend further studies on the treatment of COVID-19 patients using AQ and QZ derivatives.
- The authors in this study show that probenecid potently blocks SARS-CoV-2 replication in mammalian cells and virus replication in a hamster model. They also demonstrate that plasma concentrations up to 50-fold higher than the protein binding adjusted IC_{90} value are achievable for 24 hours following a single oral dose. Their findings support the potential clinical utility of probenecid to control SARS-CoV-2 infection in humans.

Epidemiology

- This survey aimed to estimate the seroprevalence of SARS-CoV-2 among blood donors in Kenya from January to March 2021. The authors had previously estimated it to be 4.3% in April to June 2020 and 9.1% in August to September 2020. The current study involved a total of 3018 blood samples, out of which 1333 were seropositive; crude seroprevalence was 44.2% (95% CI 42.4%-46.0%). Using Bayesian post stratification, the adjusted estimate of seroprevalence among those aged 16 to 64 years in Kenya was 48.5% (95% CI, 45.2%-52.1%). Their findings suggest SARS-CoV-2 had progressed rapidly across Kenya by February 2021, before a large third wave of infections began in March 2021.
- This multicentre cohort study reports on one-year outcomes of critical care patients post COVID-19 multisystem inflammatory syndrome in Children (MIS-C). The authors report the outcomes of 68 patients. There were no deaths, and 2 patients (3%) had critical care readmission. Both readmissions were unrelated to complications of MIS-C or immunomodulatory therapy. They found that majority of patients had good outcomes with no significant medium- or long-term sequelae.
- This cross-sectional study described which symptoms were reported with new loss of taste or smell among individuals with and without SARS-CoV-2 infection. The authors analysed data from 59153 responses that were collected from the Centers for Disease Control and Prevention's Coronavirus Self-checker. Their findings suggest that differences in symptoms occurring with new loss of taste or smell were seen between groups based on SARS-CoV-2 test positivity. In both groups, muscle aches or body aches, mild or moderate difficulty breathing, vomiting or diarrhoea, and congestion or runny nose

were associated with a new loss of taste or smell. However, in both groups with positive and negative test results, congestion or runny nose had strong associations with new loss of taste or smell, suggesting the latter may not be a valid marker of test positivity.

- This cohort study aimed to compare the characteristics of SARS-CoV-2 spread in children, aged 0 to 9 years, in 2 periods when different SARS-CoV-2 variants were circulating in Israel. Their results demonstrate that SARS-CoV-2 spread more effectively and more rapidly among young children during the time of B.1.1.7 variant circulation. Transmission rates from children aged 0 to 9 years to other contacts were doubled, highlighting the importance of making COVID-19 vaccine available for young children. They recommend to health authorities in different regions to anticipate this occurrence and implement measures to reduce spread in young children both in schools and at home.
- This population based nested case-control study aimed to determine the risk of hospital admission with COVID-19 and severe COVID-19 among teachers and their household members, overall and compared with healthcare workers and adults of working age in the general population in Scotland between March 2020 and July 2021. The authors report that teachers and their household members were not found to be at increased risk of hospital admission with COVID-19 and were found to be at lower risk of severe COVID-19 when compared with adults of working age who are otherwise similar. Their findings should reassure those who are engaged in face-to-face teaching.
- This study characterised the convalescent humoral and cellular immune response in a cohort of 91 primary school-aged children compared with 154 adults taking part in the SARS-CoV-2 Surveillance in School Kids (sKIDs) study. The authors demonstrate a markedly different profile of immune response after SARS-CoV-2 infection in children compared to adults. Their findings have potential implications for understanding immune responses to infection in children including SARS-CoV-2 multisystem inflammatory syndrome (MIS-C). They can also be used to guide and interpret the introduction of COVID-19 vaccination for children. [*not peer reviewed*]

Infection Prevention and Control

- The authors in this study formulated a novel hand gel based on zinc-aminoclay (ZnAC) and *Opuntia humifusa* (*O. humifusa*) extract, which is a high moisturizing agent. The hand gel with 0.5 wt % ZnAC and 1.0 v/v% *O. humifusa* extract can kill more than 99% *Escherichia coli* and *Staphylococcus aureus*. Toxicity evaluation shows that, the hand gel does not affect the viability of mammalian HaCaT cells. Owing to the high antimicrobial activity and skin protection of hand gels, they are suitable to be used as hand sanitizers in restaurants, hospitals, and homes effectively.
- This study investigated the impact of portable air filtration (PAF) units in a mock classroom, as a supplement to background ventilation, on localised and whole-room surface deposition and particle concentration. The experiments were conducted in the Well Living Lab in Rochester, Minnesota, USA. The authors found that PAF units could reduce air particle concentrations by a factor of 2.5 and reduce particle deposition on horizontal surfaces. [*not peer reviewed*]

Non-pharmaceutical interventions, social distancing

- This study used a decision analytical model of the COVID-19 epidemic to investigate potential outcomes if actual policies enacted in March 2020 (1st wave of the epidemic) in the St Louis region of Missouri had been delayed. Their results suggest that timely social distancing policies were associated with improved population health outcomes, and small delays may likely have led to a COVID-19 epidemic similar to the most heavily affected areas in the US. These findings indicate that an open-source modelling platform designed to accept user-supplied local and regional data may provide projections tailored to, and more relevant for, local settings.
- This study combined viral genomics and population mobility data to analyse the emergence and outbreak trajectory of SARS-CoV-2 in Bangladesh. The authors sequenced 67 viral genomes from six administrative areas (divisions) of Bangladesh in 2020. Their results indicate that there were repeated international importations until late March which were followed by a period of sustained community transmission that was consistent with mass migrations out of cities and return of transient workers to rural villages once work opportunities shut due to stay-at-home orders. They emphasize that non-

pharmaceutical interventions (such as stay at home orders) that have been successful in high-income country settings can't always be applied identically in low and middle-income countries.

- This modelling study simulated outbreaks in long-term care facility (LTCF) populations with differing vaccination coverage and non-pharmaceutical interventions (NPI) adherence to evaluate their interacting effects. The authors found that vaccination combined with strong NPI adherence produced the least morbidity and mortality. Healthcare worker vaccination improved outcomes in unvaccinated LTCF residents but was less impactful with declining NPI adherence.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 9th September 2021, Sinovac Biotech announced the launch of a phase 3 multicentre clinical trial of its Covid-19 vaccine in children and adolescents. The study will evaluate the efficacy, immunogenicity and safety of the CoronaVac vaccine on children and adolescents aged 6 months to 17 years. This multicentre, randomised, double-blind, placebo-controlled global phase III trial will enrol 14,000 participants across Chile, Philippines, Malaysia and **Kenya**, including 2,000 in **South Africa**. Eligible subjects will receive two doses of Sinovac's CoronaVac vaccine or a placebo, 28 days apart. Sinovac in collaboration with South African company Numolux Group will conduct the phase III clinical trial in South Africa. Clinical trial registration #: DOH-27-082021-6331
- On 8th September 2021, Novavax announced enrolment of the first participants in a Phase 1/2 study of a combination vaccine using its seasonal influenza and Covid-19 vaccines. The phase 1/2 clinical trial combines Novavax' recombinant protein-based NVX-CoV2373 and NanoFlu™ vaccine candidates and patented saponin-based Matrix-M™ adjuvant in a single formulation (COVID-NanoFlu Combination Vaccine). It will evaluate the safety, tolerability and immune response of the COVID-NanoFlu Combination Vaccine in 640 healthy adults aged 50 to 70 years in Australia. Both NVX-CoV2373 and NanoFlu have previously demonstrated strong results as standalone vaccines in Phase 3 clinical trials. Clinical trial registration #: NCT04961541

Therapeutics trials:

- On 8th September 2021, AIM ImmunoTech announced that it has submitted a Pre-Investigational New Drug application (Pre-IND) to the U.S. Food and Drug Administration (FDA) to study Ampligen as a potential infusion therapy for Post-COVID-19 Cognitive Dysfunction (PCCD). The company anticipates to conduct a phase 2, two-arm, randomised, double-blind, placebo-controlled, multicentre trial to assess the efficacy and safety of Ampligen in 80 subjects with PCCD. Eligible subjects will be randomised 1:1 to receive twice weekly infusions of Ampligen or placebo for a period of 12 weeks.
- On 2nd September 2021, Quantum Leap Healthcare Collaborative (QLHC) announced the interruption of the I-SPY COVID Trial aiming to evaluate famotidine celecoxib combination agents because the combined treatment failed to significantly reduce time to recovery or mortality in critically ill Covid-19 patients. I-SPY is an open-label, adaptive platform Phase II trial conducted to assess various therapies in critically ill Covid-19 patients on high-flow oxygen or mechanical ventilation. The Famotidine Celecoxib combination was chosen for evaluation because of their anti-histamine and anti-inflammatory mechanism of action. Evaluation of famotidine celecoxib included 23 sites. Clinical trial registration #: NCT04488081
- On 2nd September 2021, Adamis Pharmaceuticals announced the beginning of subject dosing in the Phase 2/3 clinical trial of an oral antiviral product candidate, Tempol, for the treatment of COVID-19. This adaptive, randomised, double-blind, placebo-controlled, phase 2/3 clinical trial will enrol 248 high risk unvaccinated subjects with early COVID-19 infection aged 18 years and older. Subjects with COVID-19 infection within five days of study entry and at least one comorbidity such as hypertension, diabetes, obesity, cancer, chronic renal disease or immunodeficiency will be randomised 1:1 to receive either Tempol or placebo. The primary endpoint is the rate of hospitalization for patients receiving Tempol, versus those receiving placebo. Clinical trial registration #: NCT04729595

- On 2nd September 2021, Sorrento Therapeutics announced that it has begun enrolment of subjects in Phase 2 clinical trial of human allogeneic adipose-derived mesenchymal stem cells (COVI-MSC) in COVID-19 patients with acute respiratory distress (ARD) or acute respiratory distress syndrome (ARDS) in Brazil. Mesenchymal stem cells have been shown to support resolution of symptoms in multiple disease settings and have the potential to reduce the long-term effects associated with pulmonary tissue damage. This multi-arm, randomised, placebo-controlled Phase 2 study will enrol 100 subjects to evaluate the efficacy and safety of COVI-MSCs in patients with COVID-19-induced ARD or ARDS. Clinical trial registration #: NCT04903327
- On 1st September 2021, MSD and Ridgeback Biotherapeutics announced the commencement of phase 3 MOVe-AHEAD clinical trial to evaluate their oral drug, molnupiravir, for the prevention of COVID-19 infection. Molnupiravir is an investigational, orally administered ribonucleoside analog that inhibits the replication of multiple RNA viruses such as SARS-CoV-2. MOVe-AHEAD is a Phase 3 multicentre, randomised, double-blind, placebo-controlled study to assess the efficacy and safety of molnupiravir in preventing Covid-19 spread within households. The trial aims to enrol about 1,332 participants aged at least 18 years and residing in the same household as someone with symptomatic laboratory-confirmed SARS-CoV-2 infection. The trial is anticipated to be carried out in Argentina, Brazil, Colombia, France, Guatemala and the US. Clinical trial registration #: NCT04939428
- On 1st September 2021, Code Pharma announced the initiation of phase 2 double-blind controlled study for its ant-viral drug, Codivir, for the treatment of COVID 19. This comes after positive results from phase 1 trial demonstrated that Codivir has a high safety profile while significantly suppressing viral replication in patients with an antiviral effect in as early as three days. Phase 2 trial is planned to be conducted in Spain, Brazil, **South Africa**, and Israel, with a larger cohort. Codivir is a short synthetic 16 amino-acid peptide derived from the HIV-1 integrase with a direct antiviral effect against SARS-CoV-2 and other RNA viruses. Clinical trial registration #: NCT04930861
- On 30th August 2021, OPKO Health announced the completion of enrolment of subjects in its Phase 2 REsCue clinical trial of Rayaldee (calcifediol) extended-release capsules to treat mild-to-moderate Covid-19 in the US. A total of 171 participants have been enrolled, including stage 3 or 4 chronic kidney disease (CKD) patients who are at an increased risk of disease progression. The trial's primary efficacy endpoints are the attainment of 25-hydroxyvitamin D level in a range between 50-100 ng/mL and time to resolution of COVID-19 symptoms. Secondary endpoints include incidence of emergency room, oxygen saturation below 94%, need for and duration of hospitalization, requirement for mechanical ventilation, mortality rate, severity and duration of illness evidenced by quality-of-life and biochemical measures. Topline data are expected later this year. Clinical trial registration #: NCT04551911

Immunotherapies trials:

- On 1st September 2021, ExeVir announced the enrolment of the first patients in a global phase 1b/2 clinical trial of its potent Covid-19 neutralising antibody, XVR011. The two-part Phase 1b/2 trial will evaluate the safety and efficacy of XVR011 in neutralising the SARS-CoV-2 virus in mild to moderate COVID-19 hospitalized patients. Phase Ib part will enrol up to 27 subjects and analyse three different intravenous doses of XVR011 with as primary endpoint the proportion of patients with adverse events. Viral load, need for oxygen supplementation, clinical score (8-point ordinal scale) and other measures of clinical activity will be the secondary endpoint. Phase 2 will enrol up to 252 patients. Clinical trial registration #: NCT04884295

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 3rd to 10th September 2021.

Country	PHSM Trend	PHSM Change
Tier 4 (High Alert): Daily case incidence per 1M people/day ≥ 80 and/or positivity rate ≥ 12%		
Botswana	↓	Officials in Botswana have eased some COVID-19 measures. Public gatherings are permitted to resume with protective measures in place, the nightly curfew was shortened by 2 hours, and the ban on the sale of alcohol was lifted.
Eswatini	↓	Schools reopened in Eswatini, although some students had to be turned away at the door in order to maintain the COVID-related capacity limitations of 20 pupils per classroom.
South Africa	↓	South Africa will move to a lockdown level 2 (from level 3), which includes the easing of many restrictions. The nightly curfew will be shortened, the capacity limits on public gatherings will be increased, and the hours during which alcohol sales are permitted will be lengthened.
Tier 3 (Moderate Alert): Daily case incidence per 1M people/day is 20 to <80 and/or positivity rate is 5% to <12%		
Nigeria	↑	In Nigeria, people living in the southern states of Edo and Ondo will need to show proof of vaccination to access public places such as banks and religious buildings starting in mid-September.
Tier 2 (Low Alert): Daily case incidence per 1M people/day is 5 to <20 and/or positivity rate is 3% to 5%		
Egypt	↓	Schools in Egypt reopened for the new academic year with stringent protective measures in place, including social distancing, improved ventilation, and students will now have hybrid schedules where they only come to in-person classes on certain days.
Zimbabwe	↑/↓	State employees in Zimbabwe have been told to either get vaccinated or resign. Zimbabwe has also eased COVID-19 restrictions from a level 4 alert to a level 2 alert, which now permits public gatherings of up to 100 people and reduces curfew times.
Tier 1 (Standard Precautions): Daily case incidence per 1M people/day is <5 and/or positivity rate is <3%		
Congo	→	Officials in Congo extended the health-related state of emergency orders until at least 24 September 2021. Ongoing measures include a ban on public gatherings of 3 or more people, nightly curfews in Brazzaville and Pointe-Noire, and closure of land and river borders.
Madagascar	↓	Madagascar ended its 17-month state of emergency for the first time since the beginning of the pandemic.

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

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