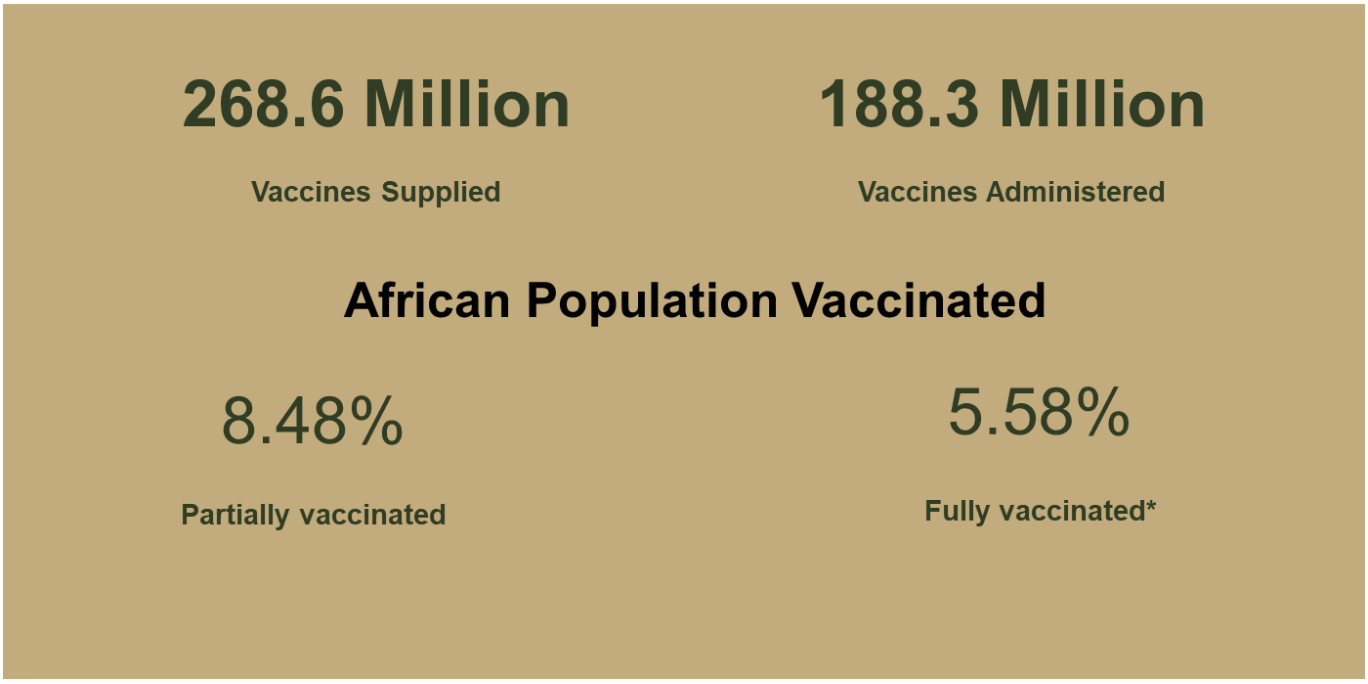
COVID-19 Scientific and Public Health Policy Update[1] – (27 October 2021)

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

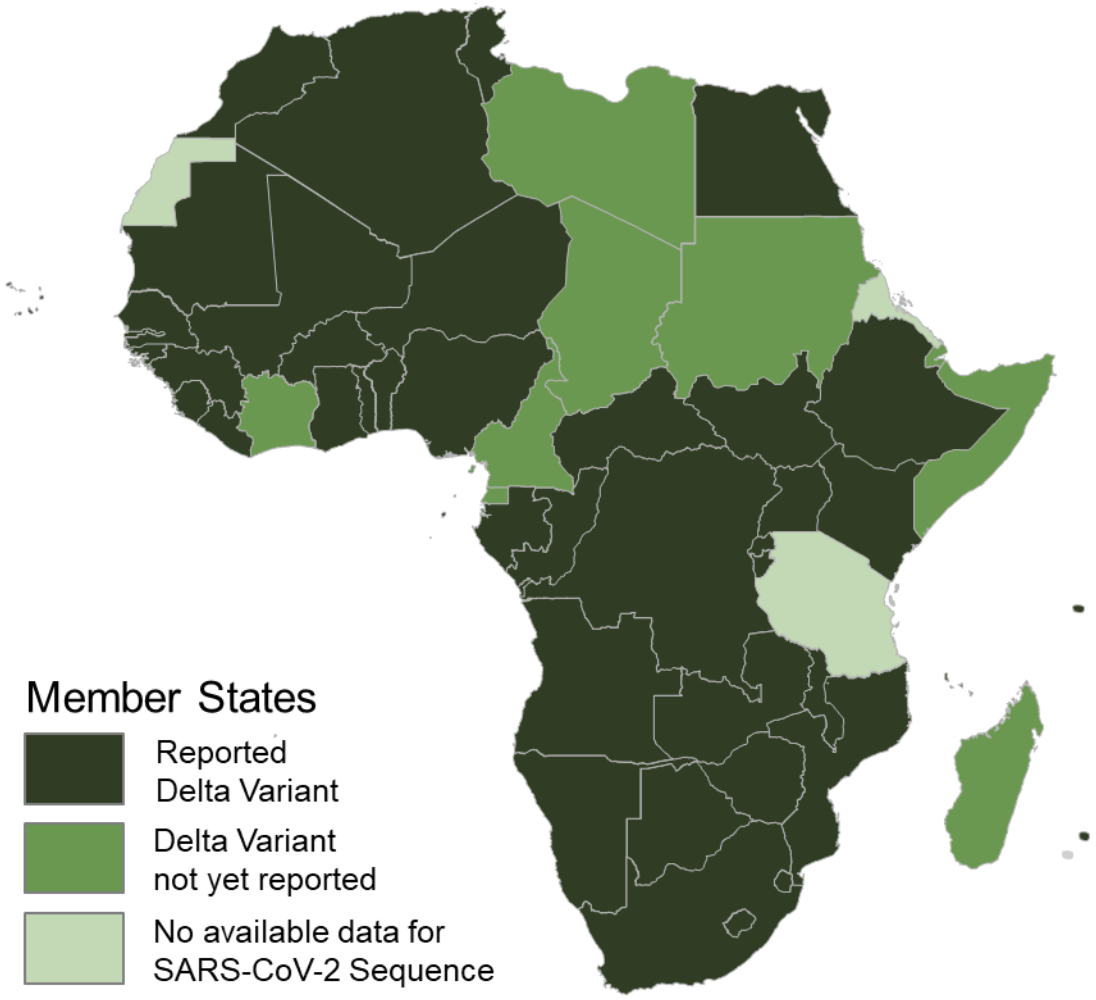


*Received two doses/ one dose of Johnson & Johnson vaccine
https://africacdc.org/covid-19-vaccination/
Updated 27th October, 2021

[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 193 countries worldwide; 41 Member States in Africa have reported this variant. https://africacdc.org/institutes/africa-pathogen-genomics-initiative/



Updated 27th October, 2021

B. New guidelines and resources

Since 9th October 2021,

- Africa CDC[2] has published new guidance and resources on:
  - Outbreak Brief 92: Coronavirus Disease 2019 (COVID-19) Pandemic

- U.S. CDC[3] has published new guidance and resources on:
  - Standard Operating Procedure (SOP) for Triage of Suspected COVID-19 Patients in non-US Healthcare Settings: Early Identification and Prevention of Transmission during Triage
  - Operational considerations for personal protective equipment in the context of global supply shortages for COVID-19 pandemic: non-US healthcare settings
  - Evaluation for SARS-CoV-2 testing in animals

[2] Africa CDC: Africa Centres for Disease Control and Prevention
[3] U.S. CDC: United States Centers for Disease Control and Prevention

- Interim Public Health Recommendations for Fully Vaccinated People
- Interim Guidance for Case Investigation and Contact Tracing in K-12 Schools
- Guidance for COVID-19 Prevention in Kindergarten (K)-12 Schools

- WHO[4] has published new guidance and resources on:
  - Interim recommendations for use of the inactivated COVID-19 vaccine, CoronaVac, developed by Sinovac
  - Coadministration of seasonal inactivated influenza and COVID-19 vaccines
  - WHO SPRP 2021 Mid-term Report - WHO Strategic Action Against COVID 19
  - WHO COVID-19 SPRP: Updated Appeal September 2021 - March 2022
  - Infection prevention and control in primary care: a toolkit of resources
  - An overview of infodemic management during COVID-19, January 2020–May 2021
  - Guidance on selecting, commissioning and using freeze-preventative vaccine carriers

- U.S. FDA[5] has issued press releases on:
  - On 26th October, FDA issued an EUA for the Celltrion DiaTrust COVID-19 Ag Home Test, an OTC COVID-19 diagnostic antigen test
  - On 26th October, FDA reissued the EUA for the Quidel QuickVue At-Home OTC COVID-19 Test
  - As of 26th October, 420 tests and sample collection devices are authorized by the FDA under emergency use authorisations (EUAs)
  - On 20th October, FDA takes additional actions on the use of a Booster Dose for COVID-19 Vaccines

- ECDC[6] has issued new resources on:
  - Options for the use of rapid antigen tests for COVID-19 in the EU/EEA and the UK - first update
  - Coronavirus disease 2019 (COVID-19) Contact Tracing Reporting Protocol, Version 1
  - COVID-19 surveillance guidance - Transition from COVID-19 emergency surveillance to routine surveillance of respiratory pathogens
  - Facilitating COVID-19 vaccination acceptance and uptake in the EU/EEA

- PHE[7] has issued new guidance and press releases on:
  - Test to Release for international travel: minimum standards for testing
  - How to do a coronavirus (COVID-19) rapid lateral flow test at home
  - Travel to England from another country during COVID-19
  - Workplace testing: terms and conditions
  - Coronavirus (COVID-19) PCR home test kit instructions
  - COVID-19 test validation approved products
  - COVID-19 vaccination: booster dose resources

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

[4] WHO: World Health Organization
[5] U.S. FDA: United States Food and Drug Administration
[6] ECDC: European Centre for Disease Prevention and Control
[7] PHE: Public Health England

C. Scientific updates

Basic Science

- This flow cytometric survey aimed to characterise SARS-CoV-2–reactive mCD4⁺ and mCD8⁺ T cell responses in tonsillar lymphoid tissue and matched peripheral blood samples. The samples were obtained from children and adults in Sweden before the current pandemic (from 2015 to 2018). The authors found that SARS-CoV-2–specific CD8⁺ T cells were more readily detected in the tonsils compared with the blood and displayed a resident memory phenotype but were less functional than CD8⁺ T cells specific for other viruses. They recommend further studies to determine whether these pre-existing cells lead to early viral containment, potentially mitigating the course of COVID-19.
- The authors in this prospective observational monocentric study among 134 patients in France analysed a panel of plasma inflammatory and anti-inflammatory cytokines and measured monocyte dysregulation via their membrane expression of HLA-DR. They found that higher blood IL-6 levels, lower quantitative expression of HLA-DR on blood monocytes and higher IL-6/ mHLA-DR ratios were statistically associated with the risk of severe forms of the disease and among the latter with death and the early onset of secondary infections.
- The authors in this study conducted *in vitro* and *in vivo* experiments in mice and rats involving infectious wild type SARS-CoV-2, B.1, B.1.1.7, B.1.351, P.3, and B.1.617.2. The study was conducted in Hong Kong. Their results reveal that the SARS-CoV-2 variant, B.1.1.7, as well as other N501Y-carrying variants including B.1.351 and P.3, has gained the capability to expand species tropism to murines and public health measures including stringent murine control should be implemented to facilitate the control of the ongoing pandemic.
- This multicentre prospective cohort study of 589 healthcare workers in the UK aimed to track T cell and SARS-CoV-2 neutralising antibody (NAb) responses after the first dose of BNT162b2 mRNA vaccine, and compare the magnitude of the responses 4 weeks after dose 2 between short and long vaccination regimens. Their results show that a single dose induces Nab responses and a sustained B and T cell response to spike protein. NAb levels were higher after the extended dosing interval (6-14 weeks) compared to the conventional 3–4-week regimen, accompanied by enrichment of CD4⁺ T cells expressing IL2. Prior SARS-CoV-2 infection amplified and accelerated the response. Their findings indicate that extension of the dosing interval is an effective, immunogenic protocol.
- This systematic review, which was conducted in Brazil, discusses the recent data showing the association of COVID-19 severity with the correct balance between the Interferon types and other cytokines for a favourable clinical outcome during infection by SARS-CoV-2.
- This study aimed to evaluate the neutralisation and binding activities of sera collected from 30 COVID-19 mRNA vaccine recipients against current SARS-CoV-2 Variants of Concern/Interest. The authors measured neutralisation activity against seven replication-competent SARS-CoV-2 isolates derived from recent clinical specimens in New York City. Their findings suggest that mRNA SARS-CoV-2 vaccines may remain effective against these viral variants of concern/interest and that spike binding antibody tests likely retain specificity in the face of evolving SARS-CoV-2 diversity.

Vaccines

- This phase 1/2 open-label clinical trial aimed to assess the safety, reactogenicity, and immunogenicity of homologous and heterologous booster vaccination in persons who had received an EUA COVID-19 vaccine regimen. The study was conducted among 458 adults at 10 U.S. sites. Participants received one of three vaccines (mRNA-1273, Ad26.COV2.S or BNT162b2). The authors found that homologous boosts provided a wide range of immunogenicity responses, with heterologous boosts providing comparable or higher titres. Reactogenicity and adverse events were similar across booster groups. Their data suggests that if a vaccine is approved or authorized as a booster, an immune response will be generated regardless of the primary COVID-19 vaccination regimen. [*not peer reviewed*]
- This case report presents details on a 17-year-old previous healthy male adolescent in Denmark who fulfilled the diagnostic criteria for multisystem inflammatory syndrome in children (MIS-C) after the 2nd dose of Pfizer-BioNTech vaccine. Differential diagnoses were thoroughly investigated and excluded,

including a previous SARS-CoV-2 infection. This case raises suspicion of a rare association between the Pfizer-BioNTech vaccine and MIS-C in a male adolescent.

- This nationwide cohort study aimed to investigate the effectiveness of heterologous ChAdOx1 nCoV-19 and mRNA prime-boost vaccination against symptomatic COVID-19 infection in Sweden. Their results showed that heterologous ChAdOx1 nCoV-19 / BNT162b2 and heterologous ChAdOx1 nCoV-19/ mRNA-1273 had 67% and 79% effectiveness against symptomatic COVID-19 infection, respectively. Also, using ChAdOx1 nCoV-19 as the first dose and an mRNA vaccine as the second dose was associated with a significantly higher effectiveness compared with the 50% effectiveness from homologous ChAdOx1 nCoV-19 / ChAdOx1 nCoV-19 vaccination. Their results support the use of heterologous vaccine schedules as an effective alternative to increase population immunity against COVID-19.
- This prospective cohort study aimed to evaluate the antibody responses in immunocompromised patients (ICPs) with diverse underlying diseases. The study involved 1002 ICPs who received the BNT162b2 mRNA vaccine in Israel. Their results showed that the proportion of participants achieving an effective antibody response two to four weeks following the second vaccine varied from 18.8% and 45% after heart and kidney transplantation, respectively, to 74.8% following stem cell transplant, 79.7% with multiple myeloma, 83.3% with solid malignancies and 98.7% in patients with HIV. Regression analysis demonstrated that age and underlying immunosuppression (except HIV), were predictors for lower titres of antibodies measured by RBD-IgG and neutralising assays.
- This qualitative study aimed to investigate and understand factors associated with facilitating and obstructing COVID-19 vaccine access and acceptance among Black and Latinx communities in the US. The authors conducted semi structured, in depth focus group discussions with 72 participants. They identified 3 themes: pervasive mistreatment of Black and Latinx communities and associated distrust; informing trust via trusted messengers and messages, choice, social support, and diversity; and addressing structural barriers to vaccination access. Their findings suggest that community-informed insights may inform health care strategies to maximize vaccine acceptance and access in communities hardest hit by the COVID-19 pandemic.

Diagnostics

- The authors in this study review current diagnostic methods for COVID-19 and propose the use of expired carbon dioxide (CO_2) as an early screening tool for SARS-CoV-2 infection. The proposed system has already been developed and tested in Malaysia. Their findings reveal that expired CO_2, also known as capnogram, can help differentiate between respiratory conditions and, therefore, could be used to detect SARS-CoV-2 infection.
- These series of experiments performed in the U.S demonstrate the use of single B cell screening for the discovery of high-affinity, potent neutralising antibodies against SARS-CoV-2. The authors methodologies can be readily extended to other highly infectious SARS-CoV-2 variants and emergent infectious diseases.
- The authors of this *in vitro* diagnostic study conducted in Korea, developed a novel isothermal nucleic acid amplification method, termed nicking and extension chain reaction system-based amplification (NESBA). They applied the NESBA technique to test 98 clinical samples for target envelope and nucleocapsid genes of SARS-CoV-2 and achieved excellent accuracy by yielding 100% sensitivity and specificity compared to qRT-PCR. Their method could serve in the point-of-care diagnosis for COVID-19.

Care and Treatment

- This multicentre, randomised clinical trial aimed to assess the effects of 12 mg/d vs 6 mg/d of dexamethasone in patients with COVID-19 and severe hypoxemia. The study was conducted at 26 hospitals in Europe and India and included 1000 adults with confirmed COVID-19 requiring at least 10 L/min of oxygen or mechanical ventilation. The authors found that treatment with 12 mg/d of dexamethasone compared with 6 mg/d of dexamethasone did not result in statistically significantly

more days alive without life support at 28 days. However, the trial may have been underpowered to identify a significant difference.

- This randomised, double-blind, placebo-controlled trial, among 657 symptomatic outpatients with COVID-19 in the US, aimed to assess whether anticoagulant or antiplatelet therapy can safely reduce major adverse cardiopulmonary outcomes. The patients were randomized in a 1:1:1:1 ratio to receive treatment with aspirin (81 mg once daily), apixaban (2.5 mg twice daily), apixaban (5.0 mg twice daily), or placebo. The authors found that treatment with aspirin or apixaban compared with placebo did not reduce the rate of a composite clinical outcome. The study was terminated because of an event rate lower than anticipated.
- This multicentre, prospective, observational cohort study at 22 intensive care units (ICUs) in the Netherlands aimed to identify respiratory sub-phenotypes of COVID-19-related acute respiratory distress syndrome (ARDS). The authors found no empirical evidence for the existence of respiratory sub-phenotypes at the start of invasive ventilation, nor at cross-sectional analysis in the succeeding 4 days. However, using time-dependent analysis, they identified two sub-phenotypes that developed during the first 4 days of invasive mechanical ventilation. Trajectories of ventilatory ratio and mechanical power were most discriminatory and modelling these parameters alone provided prognostic value for duration of mechanical ventilation and mortality.
- This double-blind, placebo-controlled, multicentre, randomised phase 2 trial aimed to evaluate safety and efficacy of oral angiotensin II type 2 receptor agonist C21 in hospitalised patients with COVID-19 and CRP ≥ 50-150 mg/L. The study was conducted at eight sites in India. The patients received 100mg bid of C21 for 7 days on top of standard of care, including glucocorticoids and remdesivir. The authors found no difference in the rate of decline of CRP in the 2 groups. A post hoc analysis showed a marked reduction of requirement for oxygen at day 14 in those randomised to C21. The day 14 results in this study justify further evaluation in a Phase 3 study which is currently underway.
- This randomised, controlled, open-label, platform trial aimed to evaluate the efficacy and safety of colchicine in patients hospitalised with COVID-19. The trial was conducted in 177 hospitals in the UK, 2 hospitals in Nepal and 2 hospitals in India, it involved 11,000 patients. The authors found that use of colchicine was not associated with a reduction in mortality, duration of hospitalisation, or the risk of being ventilated or dying for those not on ventilation at baseline. The results were consistent across the prespecified subgroups of age, sex, ethnicity, duration of symptoms before randomisation, level of respiratory support at randomisation, and use of corticosteroids. Their results do not support the use of colchicine in adults hospitalised with COVID-19.
- This cohort study aimed to examine the association between the receipt of tumour necrosis factor (TNF) inhibitor monotherapy and the risk of COVID-19–associated hospitalisation or death compared with other commonly prescribed immunomodulatory treatment regimens among adult patients with immune-mediated inflammatory diseases (IMIDs). The authors performed a pooled analysis of data from 3 international COVID-19 registries comprising of 6077 patients from 74 countries with rheumatic diseases, inflammatory bowel disease, and psoriasis. They found that TNF inhibitor monotherapy was associated with a lower risk of adverse COVID-19 outcomes compared with other commonly prescribed immunomodulatory treatment regimens.

Epidemiology

- This cross-sectional study aimed to estimate the prevalence of past SARS-CoV-2 in three high-density communities in Harare, Zimbabwe before and after the second wave of SARS-CoV-2. A total of 2340 individuals participated in the study. The authors found that SARS-CoV-2 seroprevalence was 19.0% (95% CI 15.1-23.5%) in 2020 and 53.0% (95% CI 49.6-56.4) in 2021. The prevalence ratio was 2.47 (95% CI 1.94-3.15) comparing 2020 with 2021 after adjusting for age, sex, and community. Almost half of all participants who tested positive reported no symptoms in the preceding six months. They recommend further seroprevalence surveys to understand transmission during the third wave.
- This retrospective study aimed to use whole genome sequencing to describe the molecular epidemiology of the SARS-CoV-2 outbreak and to inform the implementation of effective public health interventions for control in Zimbabwe. The authors analysed 92,299 nasopharyngeal samples collected

between 20th March and 16th October 2020. Only 8099 samples were PCR-positive and 328 were available for sequencing, with 156 passing sequence quality control. The authors identified at least 26 independent introductions of SARS-CoV-2 into Zimbabwe in the first 210 days which were associated with 12 global lineages. 151 (97%) of 156 had the Asp614Gly mutation in the spike protein. Most cases, 93 (60%), were imported from outside Zimbabwe. Community transmission was reported 6 days after the onset of the outbreak.

- This population-based, longitudinal cohort study aimed to investigate the seroepidemiology of SARS-CoV-2 among frontline hospital workers and communities in Ethiopia. Their findings show that SARS-CoV-2 infection has been widespread and highly dynamic. Their SEIR model, fitted on the basis of the current trend of seroincidence and poor adherence to mitigation strategies, has shown that front-line hospital workers at tertiary hospitals were approaching a threshold for herd immunity, even before the start of the vaccination initiative. They recommend targeting mitigation measures to the most vulnerable, including older people and those with underlying medical conditions.
- This cross-sectional study aimed to evaluate the change in rates of pregnancy complications associated with the COVID-19 pandemic period among pregnant women with commercial health insurance across the US. The authors compared 152,903 deliveries during the COVID-19 pandemic period (1st March to 31st December 2020) and 172,095 deliveries during the referent period (1st March to 31st December 2019). Compared with the referent period, the pandemic period was associated with a statistically significant higher risk of gestational diabetes (RR, 1.12; 95% CI, 1.10-1.15), gestational hypertension (RR, 1.07; 95% CI, 1.05-1.09), poor foetal growth (RR; 1.07; 95% CI, 1.03-1.11), and preeclampsia (RR, 1.04; 95% CI, 1.01-1.07).
- This cohort study aimed to investigate the association between risk of COVID-19 in nonimmune individuals and the number of their family members with known immunity acquired from a previous COVID-19 infection or full vaccination (2 vaccine doses). The study involved 1,789,728 individuals from 814,806 families in Sweden. The authors found that family members without immunity had a 45% to 97% lower risk of contracting COVID-19 as the number of immune family members increased. Their results suggest that COVID-19 vaccines play a key role in reducing the transmission of the virus within families, which likely has implications for herd immunity and pandemic control.
- This systematic review aimed to estimate organ system–specific frequency and evolution of post-acute sequelae of COVID-19 (PASC). The authors included 57 studies comprising more than 250 000 survivors of COVID-19 in their systematic review. Majority of the studies were from high-income countries (79%). They found that more than half of COVID-19 survivors experienced PASC 6 months after recovery. The most common PASC involved functional mobility impairments, pulmonary abnormalities, and mental health disorders. These long-term PASC effects must be factored into existing health care systems, especially in low- and middle-income countries.
- This prospective cohort study aimed to gain a better understanding of the possible role of children in the transmission of SARS-CoV-2. The study was conducted in Belgium among a volunteer sample of 181 children, parents, and school employees. The authors found no significant difference between the number of children and the number of adults testing positive for SARS-CoV-2 infection during the study period; children were asymptomatic significantly more often compared with adults (46% vs 13%). A reconstruction of the outbreak showed that most transmission events originated from within the school. They recommend for additional measures to be considered so as to reduce the transmission of SARS-CoV-2 at schools.
- This retrospective cohort study aimed to assess the factors associated with SARS-CoV-2 diagnosis and severe outcomes among people living with HIV. The study was conducted in Catalonia (Spain). The authors found that SARS-CoV-2 diagnosis was more common among migrants, men who have sex with men, and those with ≥4 comorbidities; whereas, severe COVID-19 was associated with older age and increased numbers of chronic comorbidities. They observed differences in the risk of severe outcomes according to CD4 cell counts in patients with detectable HIV RNA viral loads. Their results show that people with HIV with chronic comorbidities and unsuppressed HIV RNA viral load could be at increased risk of severe outcomes and should be prioritised in clinical management and SARS-CoV-2 vaccination programmes.

- This population based, multicentre cohort study aimed to understand the role of HIV infection and levels of immunity affecting the COVID-19 clinical outcomes. The study used the National COVID Cohort Collaborative (N3C) data in the USA. Their findings showed that people with HIV had higher odds of COVID-19 death (AOR 1.29, 95% CI 1.16–1.44) and hospitalisation (1.20, 1.15–1.26), but lower odds of mild or moderate COVID-19 (0.61, 0.59–0.64) than people without HIV. Interaction terms revealed that the elevated odds were higher among older age groups, male, Black, African American, Hispanic, or Latinx adults. A lower CD4 cell count (<200 cells per µL) was associated with all the adverse COVID-19 outcomes, while viral suppression was only associated with reduced hospitalisation. They recommend service strengthening and support to prevent aggravated COVID-19 outcomes among people with HIV, particularly those with profound immunodeficiency.
- This systematic review and meta-analysis conducted in China aimed to identify the predictors of unfavourable prognosis of COVID-19 in children and adolescents. The authors included 56 studies comprising 79,104 individuals. Their results show that male sex, blood group A, underlying conditions (obesity, chronic pulmonary disease, congenital heart disease and neurological diseases), and biomarkers (CRP and D-dimer level at baseline) were associated with poor prognosis in children and adolescents with COVID-19. Clinical symptoms and complications (acute respiratory distress syndrome, acute kidney injury, multisystem inflammatory syndrome in children (MIS-C), shortness of breath, gastrointestinal symptoms, and the need for intensive care) also increased the risk of certain unfavourable outcomes.

Infection Prevention and Control

- This cross-sectional study describes the single use face mask littering in Bangkok, Thailand. The authors highlight three policy implications to tackle the growing problem: raising awareness, regulation, and provision of bins designed for used face masks in strategic places and supporting innovations and research for eco-friendly face masks.
- This study analysed nosocomial infection (NI) outbreaks that occurred in three hospitals in Japan to provide insights into preventing NI outbreaks of COVID-19. The authors found that despite having authorised infection control teams and using existing standardised IPC measures, SARS-CoV-2 may still enter hospitals. Early detection of suspected cases and confirmation by PCR test, carefully dealing with staff-to-staff transmission were the most essential factors to prevent NI outbreaks. It was also suggested that ordinary training on IPC for staff does not always provide enough practical knowledge and skills. They recommend external technical and operational support in such cases.

Non-pharmaceutical interventions, social distancing

- This modelling study in South Korea analysed and measured the impact of mandatory mask wearing and practicing social distancing in preventing infection exposure in passengers during their journeys in public transport. Their results show that mandatory wearing of masks exhibits effects similar to maintaining 2-m social distancing in preventing COVID-19. Mandatory wearing of masks and practicing social distancing with masks during peak hours reduced infection rates by 93.5% and 98.1%, respectively.
- This retrospective longitudinal study investigated face mask supply under the name-based rationing system during the early phase of COVID-19 in Taiwan to understand the coverage and fairness of face mask supply. Their results show that the rationing system supplied masks fairly to the total population, can provide universal coverage, and was sufficient for daily use for the population.
- This prospective observational cohort study aimed to estimate the incidence and risk factors associated with SARS-CoV-2 seroconversion before the start of the second wave of infections in Manaus, Brazil. The authors found that the anti-SARS-CoV-2 seropositivity rate increased from 27.72% to 34.33% in the DETECTCoV-19 cohort before the second wave of COVID-19 in Manaus. They identified the following risk factors for seroconversion: having a COVID-19 case in the household (IRR 1.49 [95% CI 1.21–1.83]), not wearing a mask during contact with a person with COVID-19 (1.25 [1.09–1.45]), relaxation of physical distancing (1.31 [1.05–1.64]), and having flu-like symptoms (1.79 [1.23–2.59]) or

a COVID-19 diagnosis (3.57 [2.27–5.63]) between the first and second visits, whereas working remotely was associated with lower incidence (0.74 [0.56–0.97]).

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 26th October 2021, Pfizer and BioNTech announced that the Vaccines and Related Biological Products Advisory Committee (VRBPAC) of the US Food and Drug Administration (FDA) has recommended granting Emergency Use Authorisation (EUA) for the Pfizer-BioNTech COVID-19 vaccine, Comirnaty, in children between the age of 5 to 11 years. The decision was backed up by the scientific evidence results from a phase 2/3 randomized, controlled trial that included about 4,500 children aged 5 to <12 years of age who received a two-dose regimen of 10-µg doses administered 21 days apart. According to the trial data, the vaccine showed a favourable safety profile, robust immune responses and a vaccine efficacy rate of 90.7% in participants without prior SARS-CoV-2 infection, measured from 7 days after the second dose. Pfizer and BioNTech plan to request for authorisations from other regulatory agencies globally for the vaccine in this age range.
- On 25th October 2021, European Medicine Agency (EMA) reported that its Committee for Medicinal Products for Human Use (CHMP) has recommended a booster dose of Moderna Spikevax Covid-19 vaccine in individuals aged >18 years in the European Union. The 50µg booster dose may be administered at least six months after receiving the first two doses of the vaccine. The booster dose consists of half the dose used for the primary vaccination schedule. The agency noted that according to the current available data, the pattern of side effects after the booster is similar to what occurs after the second dose.
- On 21st October 2021, Pfizer and BioNTech announced topline results from a Phase 3 randomized, controlled clinical trial of their COVID-19 Vaccine booster dose showing a 95.6% vaccine efficacy. The phase 3 trial aimed to evaluate the efficacy and safety of a 30-µg booster dose of the Pfizer-BioNTech COVID-19 Vaccine in more than 10,000 individuals aged ≥16 years. In the trial, a booster dose administered to individuals who previously received the Pfizer-BioNTech primary two-dose series restored vaccine protection against COVID-19 to the high levels achieved after the second dose, showing a relative vaccine efficacy of 95.6% when compared to those who did not receive a booster. COVID-19 booster was also found to have favourable safety profile. According to the multiple subgroup analyses, the efficacy of the booster shot was consistent irrespective of race, ethnicity, age, sex or comorbid conditions. The companies plan to submit these data to FDA, EMA and other regulatory agencies to further support licensure in the U.S. and other countries.
- On 20th October 2021, the U.S. Food and Drug Administration reported amendment of the emergency use authorisations (EUA) for COVID-19 vaccines to allow for the use of a single booster dose of Johnson and Johnson COVID-19 Vaccine to be administered at least 2 months after completion of the single-dose primary regimen to individuals >18 years. The authorisation for emergency use of a single booster dose of the Janssen COVID-19 Vaccine is based on the FDA's evaluation of immune response data in 39 participants from a clinical trial including 24 participants who were 18 through 55 years of age and 15 participants who were 65 years of age and older. The study participants received a booster dose approximately 2 months after their first dose, and the results demonstrated a booster response and was well tolerated. The Janssen COVID-19 Vaccine will also be given as a heterologous booster dose to eligible people who have completed a primary vaccination with a different authorised or approved Covid-19 vaccine. J&J stated that the booster shot will have the same formulation and dosage strength as the initial dose.
- On 20th October 2021, Moderna announced that the U.S. Food and Drug Administration (FDA) has authorized for emergency use a booster dose of the Moderna COVID-19 vaccine (mRNA-1273) at the 50 µg dose level. The booster dose vaccine is to be used for people aged 65 and older; people aged 18 to 64 who are at high risk of severe COVID-19; and people aged 18 to 64 with frequent institutional or occupational exposure to SARS-CoV-2. It should be administered at least six months after

completion of the primary series. The FDA also authorized a single booster dose of the Moderna COVID-19 Vaccine for individuals who have completed a primary vaccination with other authorized or approved COVID-19 vaccines. The FDA based this EUA on the totality of scientific evidence shared by the company and reviewed by the FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC).

- On 18th October 2021, South African Health Products Regulatory Authority (SAHPRA) announced that it has decided not to approve Russia's Sputnik V Covid-19 vaccine due to human immunodeficiency virus (HIV) concerns in **South Africa**. This decision came after consultation with local and international scientific experts and after considering all the available data, including review of the dossier submitted by Lamar International (Pty) Ltd, locally-licenced applicant. Concerns have been raised about the safety of Ad5-vectored vaccines in populations at risk for HIV infection. Sputnik V vaccine merges two dissimilar adenovirus-vectored constructs based on Adenovirus Type 26 (Ad26) and Adenovirus Type 5 (Ad5). SAHPRA considered outcome results of the STEP and PHAMBILI trials which both trials showed that administration of an Ad5-vectored vaccine was associated with enhanced susceptibility/acquisition of HIV in men. In addition, the company could not provide additional information on the Sputnik V vaccine's safety in settings with increased HIV occurrence. However, SAHPRA said that rolling review of the Sputnik V vaccine will remain open for submission of relevant safety data in support of the application. To date, the Sputnik V COVID-19 vaccine has not received Emergency Use Listing by the World Health Organization (WHO).
- On 18th October 2021, Valneva announced positive topline results from the Phase III CoV-Compare clinical trial of its inactivated, adjuvanted COVID-19 vaccine candidate, VLA2001 which met the co-primary endpoints in adolescent and adult subjects. This randomized, observer-blind, controlled, comparative immunogenicity, phase 3, CoV-Compare trial recruited a total of 4,012 participants aged ≥18 years across 26 trial sites in the United Kingdom. According to the data, VLA2001 demonstrated superior neutralizing antibody titre levels compared to active comparator vaccine, AstraZeneca's AZD1222 (ChAdOx1-S) and had neutralizing antibody seroconversion rate above 95%. VLA2001 was well tolerated with tolerability profile significantly more favourable compared to AstraZeneca's vaccine. VLA2001 consists of inactivated whole virus particles of SARS-CoV-2 with high S-protein density, in combination with two adjuvants, alum and CpG 1018. Clinical trial registration #: VLA2001-301
- On 15th October 2021, Pfizer and BioNTech announced that they submitted data to the European Medicines Agency (EMA), supporting the use of COMIRNATY® (COVID-19 mRNA vaccine) in children between 5 to <12 years of age in the European Union (EU). The latest submission is intended to modify the Conditional Marketing Authorisation (CMA) for the vaccine in the EU. Currently, the vaccine is authorised for use under CMA from the European Commission to prevent COVID-19 in individuals aged 12 years or above. The variation request includes data from a phase 2/3 study, which is enrolling children 6 months to <12 years of age. The analysis of 2,268 subjects aged 5 to <12 years showed that SARS-CoV-2–neutralizing antibody geometric mean titre (GMT) was 95% demonstrating strong immune response in this cohort of children one month after the second dose. The vaccine was also found to be well tolerated in this group.
- On 12th October 2021, Arcturus Therapeutics announced that it has obtained approval from the Vietnam Ministry of Health to proceed into phase 3b part of the placebo-controlled, observer-blind phase 1/2/3 clinical trial for its COVID-19 mRNA vaccine, ARCT-154, targeting SARS-CoV-2 delta variant and other variants of concern. The approval follows the review of positive safety data from the initial 1,000 participants included in the Phase 1/2/3a cohorts of the ARCT-154 study. The company has started dosing subjects in the trial which will enrol up to 20,000 subjects. The subjects enrolled will either receive a two-dose regimen of ARCT-154, at 28 days apart, or a placebo. The company, along with its manufacturing partner, Vinbiocare Biotechnology, plans to seek emergency use authorisation (EUA) for the vaccine in Vietnam in December this year. Clinical trial registration #: NCT05012943
- On 11th October 2021, INOVIO announced that Colombia's National Food and Drug Surveillance Institute (INVIMA) has granted the company authorisation to conduct a phase 3 segment of the global phase 2/3 INNOVATE trial for its DNA vaccine candidate, INO-4800 for COVID-19 in Colombia. INOVIO is partnering with Advaccine Biopharmaceuticals Suzhou Company to conduct phase 3 segment of INNOVATE clinical trial in multiple countries mainly focusing in Latin America, Asia, and

Africa. The aim of the phase 3 segment of the INNOVATE trial is to evaluate the efficacy of INO-4800 in a two-dose regimen (2.0 mg per dose), administered one month apart, in a 2:1 randomisation in men and non-pregnant women ≥18 years of age. The primary endpoint of this case-driven Phase 3 trial is virologically confirmed COVID-19.

Therapeutics trials:

- On 25th October 2021, European Medicine Agency (EMA) reported that its Committee for Medicinal Products for Human Use (CHMP) has begun a rolling review of molnupiravir, oral antiviral medicine, for the treatment of COVID 19 in adults. This decision to initiate the rolling review based on preliminary results from laboratory and clinical studies which suggest that molnupiravir may reduce the ability of SARS-CoV-2 to multiply in the body, thus preventing hospitalisation or death in patients with COVID-19. The Agency will assess the quality, safety, effectiveness and compliance of molnupiravir with the usual European Union standards for effectiveness, safety and quality.
- On 18th October 2021, Cardiol Therapeutics announced the expansion of its phase 2/3 LANCER trial for its drug CardiolRx™ for treatment of hospitalised COVID-19 patients to include hospital centres in Brazil, Mexico, and Canada. CardiolRx is an oral, cannabidiol-based approach that is not extracted from botanical sources but is pharmaceutically produced. This phase 2/3 randomised, double-blind, placebo-controlled trial is designed to assess the efficacy and safety of CardiolRx™ in preventing cardiovascular complications in hospitalized COVID-19 patients at risk for, or with a prior history of, cardiovascular disease (CVD). The trial primary efficacy endpoints are the percentage difference between the active and placebo groups of patients who develop either one or more several outcomes including all-cause mortality, ICU admission and/or ventilator support, and cardiovascular complications within 28 days following randomisation and first dose of study medication. In addition, the trial is expected to generate invaluable clinical data regarding CardiolRx therapeutic potential in the treatment of other inflammatory cardiac disorders, including acute myocarditis and heart failure. Clinical trial registration #: NCT04615949
- On 13th October 2021, NeuroBo Pharmaceuticals announced that it has received recommendations from the independent Data Monitoring Committee (DMC) to continue enrolment in the phase 2/3 clinical trial of its lead oral drug candidate, ANA001 for the treatment of moderate to severe COVID-19 patients. The decision came after review of safety data of 36 patients who were treated in study. ANA001 is an oral niclosamide with antiviral and anti-inflammatory properties for treatment of patients with COVID-19. This two-part phase 2/3 multi-centre, double blind, placebo-controlled study aims to assess safety, tolerability, and efficacy of ANA001. The trial is being conducted in the United States and will enrol up to 60 subjects in phase 2 and 100 subjects in phase 3. In both phases hospitalized patients with moderate to severe COVID-19 (patients not requiring ventilators) receive a seven-day course of ANA001 in addition to standard-of-care treatment. Clinical trial registration #: NCT04603924
- On 11th October, 2021, AstraZeneca reported positive results from TACKLE phase 3 COVID-19 treatment trial meeting its primary endpoint for its long acting antibody (LAAB) combination, AZD7442, for treating COVID 19 patients. This phase III, randomised, double-blind, placebo-controlled, multi-centre TACKLE trial enrolled 903 subjects aged ≥18 years randomized in a ratio of 1:1 to receive either a dose of 600mg of AZD7442 or saline placebo administered in two separate, sequential IM injections. Analysis from 822 participants demonstrated that AZD7442 statistically significant reduced severe COVID-19 or mortality by 50% compared to placebo in mild-to-moderate symptomatic COVID-19 patients in outpatient settings. AZD7442 was also found to be well tolerated. Clinical trial registration #: NCT04723394
- On 11th October 2021, Merck and Ridgeback Biotherapeutics announced that Merck has submitted an emergency use authorisation (EUA) application to the US Food and Drug Administration (FDA) for its investigational oral antiviral medicine, molnupiravir (MK-4482/EIDD-2801), to treat COVID-19. Molnupiravir is an investigational, orally-administered potent ribonucleoside analogue that can prevent

the SARS-CoV-2 virus replication. The EUA submission is based on positive results from the interim analysis of the Phase 3 MOVe-OUT clinical trial, which evaluated molnupiravir in non-hospitalized adult patients with mild-to-moderate COVID-19 at risk for progressing to severity or hospitalisation. The interim analysis showed that molnupiravir reduced the risk of hospitalisation or death by approximately 50% and nearly 7.3% of patients enrolled were in hospital or died by day 29 compared to 14.1% of patients treated with placebo. The two companies are working to submit applications for emergency use or marketing authorisation of molnupiravir with regulatory agencies across the world in the coming months.

Immunotherapies trials:

- On 8th October 2021, Brii Biosciences reported that it has filled an emergency use authorisation (EUA) application with the US Food and Drug Administration (FDA) for its combination therapy, BRII-196/BRII-198, to treat Covid-19 patients. BRII-196 and BRII-198 are non-competing SARS-CoV-2 monoclonal neutralizing antibodies derived from convalesced COVID-19 patients designed to treat non-hospitalised COVID-19 patients at high risk of clinical progression to severe disease. The EUA filing is based on positive results from the NIH-sponsored Phase 3 clinical trial, ACTIV-2, in which the BRII-196/BRII-198 combination demonstrated a 78%statistically significant reduction of hospitalisation and death and improved safety over placebo in non-hospitalized COVID-19 patients at high risk of clinical progression to severe disease. The trial was funded by the National Institutes of Health (NIH), and was conducted at clinical trial sites in Brazil, South Africa, Mexico, Argentina, the Philippines and the US.

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 11th to 18th October 2021.

Country	PHSM Trend	PHSM Change
Tier 4 (High Alert): Daily case incidence per 1M people/day ≥ 80 and/or positivity rate ≥ 12%		
Eswatini	↓	Authorities relax domestic COVID-19 measures; while curfew remains; places of worship, sports activities, social gatherings etc. are permitted with capacity limits and restrictions on the sale of alcohol.
Reunion	↓	Capacity limits for businesses and markets have been lifted; the curfew is no longer in effect; and gatherings of up to 10 people are allowed in public spaces. Restaurants and entertainment venues are still operating at 50% capacity and facemasks are mandatory in most public spaces.
Senegal	↓	Authorities eased COVID-19 restrictions; businesses, entertainment venues and public transport are allowed to operate at full capacity, provided people wear masks. International travel has resumed for all travellers producing a negative COVID-19 PCR test issued within 5 days of travel.

Rwanda	↑/↓	Gyms and fitness centres are open, private businesses, restaurants, bars and entertainment venues may reopen at full capacity under strict health guidelines and proof of vaccination requirements; public offices remain restricted to operating at 75%; Curfew remains in place but no quarantine on arrival
Lesotho	↓	Curfew has been reduced to 0:00 - 4:00 AM; restaurants may operate at 50% capacity; entertainment and sports venues may operate at full capacity if patrons show proof of vaccination, facemasks remain mandatory in public spaces.
Namibia	↓	Officials have relaxed certain measures through November 15, 2021; the curfew has been suspended and gatherings restrictions have been relaxed; limits for public gatherings increased from 150 - 200 and bars/restaurants are permitted to operate at 50% capacity.
Tier 3 (Moderate Alert): Daily case incidence per 1M people/day is 20 to <80 and/or positivity rate is 5% to <12% (No Data Available)		
Tier 2 (Low Alert): Daily case incidence per 1M people/day is 5 to <20 and/or positivity rate is 3% to 5%		
Guinea-Bissau	→	Authorities have extended the state of calamity until 26th October 2021.
Sao Tome and Principe	→	Authorities have extended COVID-19 measures through 31st October 2021.
Togo	↓	Domestic measures have eased with bars and places of worship reopening without capacity limits; vaccination campaign is in full swing with vaccine requirements in place to enter public buildings. Masks remain mandatory and social gatherings continue to be restricted. International travel restrictions remain largely unchanged
Tier 1 (Standard Precautions): Daily case incidence per 1M people/day is <5 and/or positivity rate is <3%		
Congo	→	Authorities extended state of emergency until 1st November 2021
Tier 0 (No Data Available)		

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