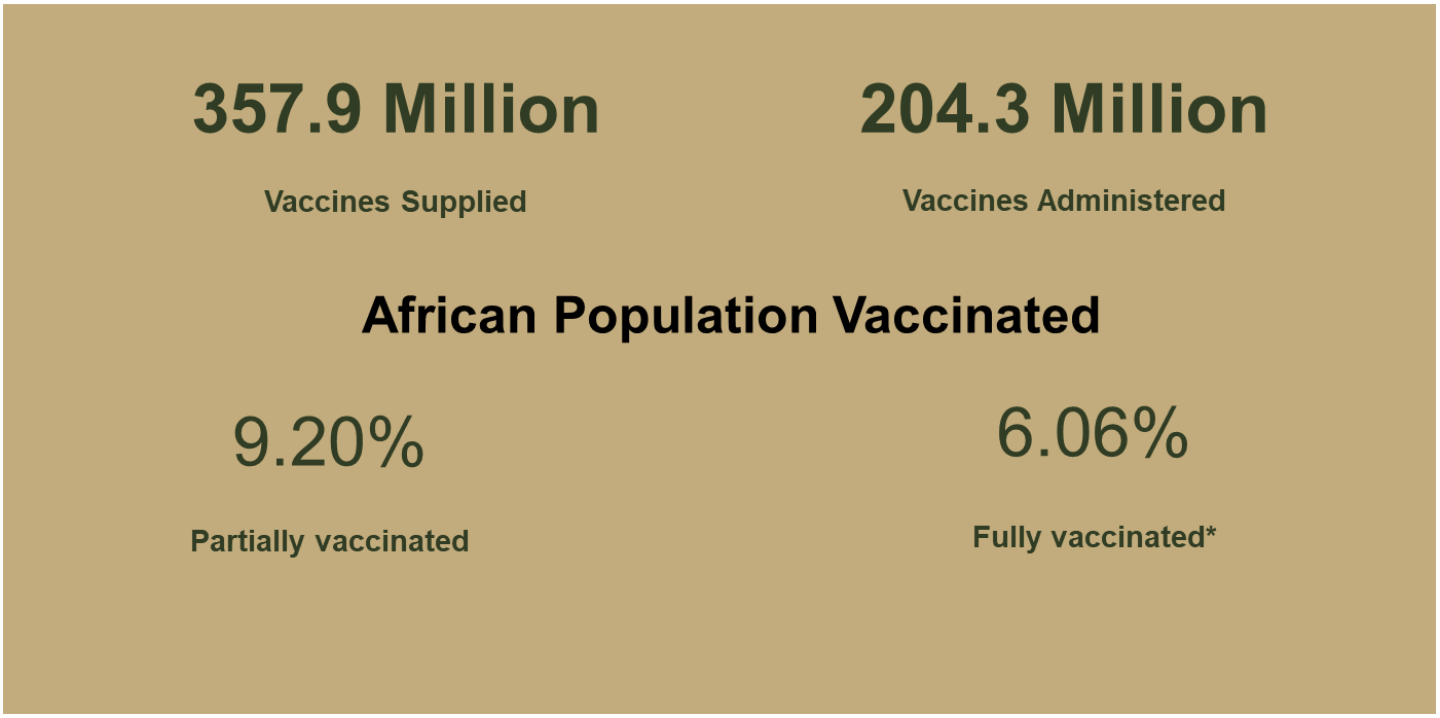
# COVID-19 Scientific and Public Health Policy Update[1] – (10 November 2021)

*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**

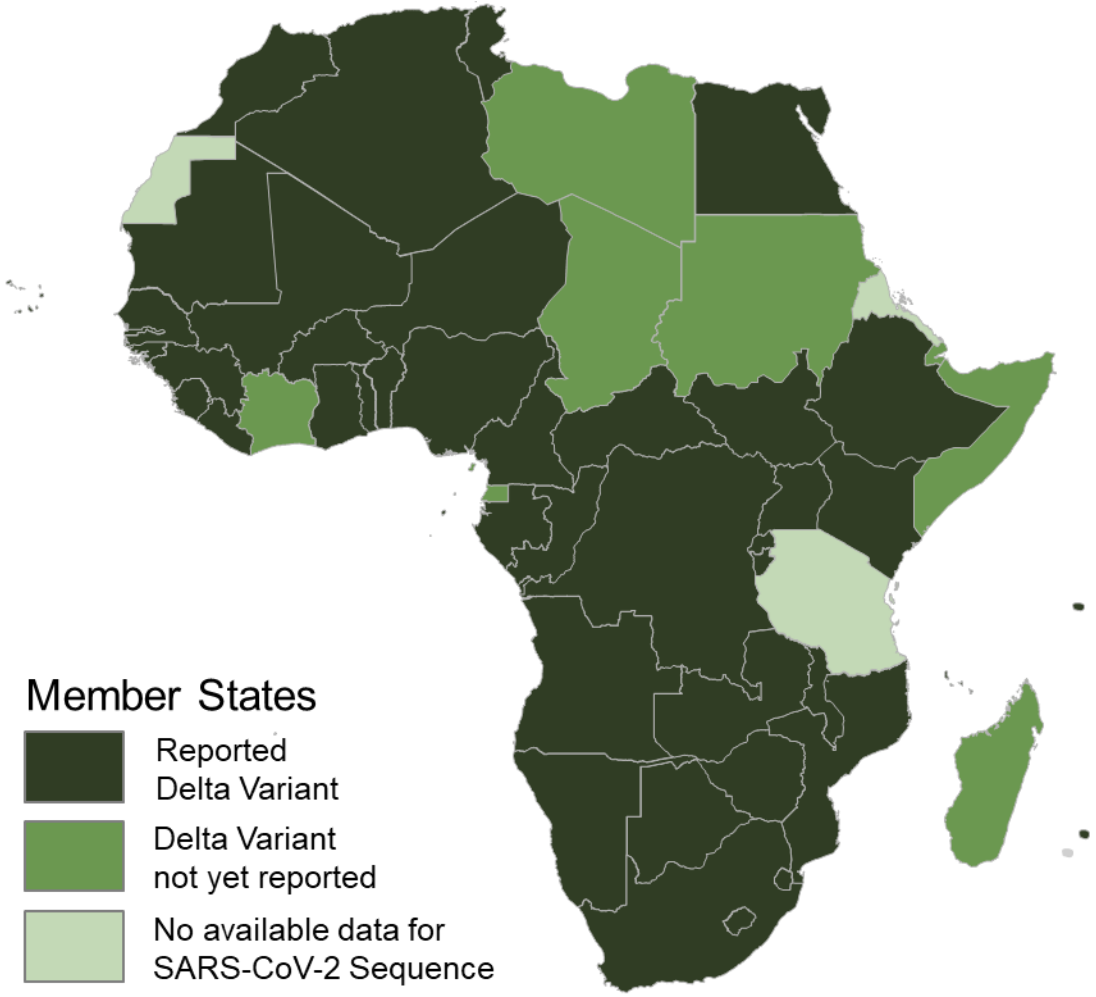



*Received two doses/ one dose of Johnson & Johnson vaccine
https://africacdc.org/covid-19-vaccination/
Updated 10th November, 2021

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




Updated 10th November, 2021

## B. New guidelines and resources

**Since 23rd October 2021,**

- Africa CDC[2] has published new guidance and resources on:
  - Guidance for Establishing a National Laboratory Quality Framework
  - Finding the Balance: Public health and social measures in Tunisia
  - Outbreak Brief 92: Coronavirus Disease 2019 (COVID-19) Pandemic

- U.S. CDC[3] has published new guidance and resources on:
  - COVID-19 Guidance for Operating Early Care and Education/Child Care Programs
  - Considerations for Institutes of Higher Education

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

- Operational Considerations for Personal Protective Equipment in the Context of Global Supply Shortages for Coronavirus Disease 2019 (COVID-19) Pandemic: non-US Healthcare Settings
- Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 (COVID-19)
- Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19

- WHO[4] has published new guidance and resources on:
  - Injection safety in the context of coronavirus disease vaccination
  - Key planning recommendations for mass gatherings in the context of COVID-19
  - Interim recommendations for use of the Bharat Biotech BBV152 COVAXIN® vaccine
  - Background document on the Bharat Biotech BBV152 COVAXIN® vaccine
  - WHO strategy for engaging religious leaders, faith-based organizations and faith communities in health emergencies
  - Interim recommendations for an extended primary series with an additional vaccine dose for COVID-19 vaccination in immunocompromised persons

- U.S. FDA[5] has issued press releases on:
  - On 5th November, FDA issued an EUA for the iHealth COVID-19 Antigen Rapid Test, an OTC COVID-19 antigen diagnostic test that delivers results in 15 minutes
  - As of 5th November, 419 tests and sample collection devices are authorized by the FDA under emergency use authorizations
  - On 29th October, FDA issued and EUA for the Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 to include children 5 -11 years of age

- ECDC[6] has issued new resources on:
  - COVID-19 Contact Tracing Reporting Protocol, Version 1
  - Contact tracing in the EU: public health management of persons, including healthcare workers, who have had contact with COVID-19 cases – fourth update
  - Options for the use of rapid antigen tests for COVID-19 in the EU/EEA and the UK - first update

- PHE[7] has issued new guidance and press releases on:
  - COVID-19 vaccination: booster dose resources
  - COVID-19 vaccination: British Sign Language resources
  - Approved COVID-19 vaccines and countries and territories with approved proof of vaccination

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 molecular study conducted in the USA shows that SARS-CoV-2 virus-like particles (SC2-VLPs) can package and deliver exogenous transcripts, enabling analysis of mutations within all structural proteins and at multiple steps in the viral life cycle. In SC2-VLPs, four nucleocapsid (N) mutations found universally in more-transmissible variants independently increased mRNA delivery and expression. SC2-VLPs provide a platform for rapid testing of viral variants outside a biosafety level 3 setting and

[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

demonstrate N mutations and particle assembly to be mechanisms that could explain the increased spread of variants, including Delta.

- This prospective cohort study aimed to characterise systemic and mucosal antibody production during the first 2 months of life among infants who were born to mothers infected with SARS-CoV-2. The study involved 21 pregnant women who gave birth at Policlinico Umberto I in Rome, Italy, from November 2020 to May 2021, and their newborns. The authors found that infants who received breastmilk during the first 2 months of life had significantly higher spike-specific salivary IgA antibody levels compared with formula-fed infants. They detected IgA spike immune complexes in breastmilk. Their findings suggest that maternal protection goes beyond passive immunity, with immune complexes in breastmilk stimulating the active development of the neonatal immune system.
- This gene co-expression network analysis performed in Iran aimed to discover novel potential drugs for treatment of SARS-CoV-2 disease. The authors expected that the drugs introduced to treat SARS-CoV coronavirus would also be effective in treating SARS-CoV-2 disease. Their findings suggest that fluorouracil, cisplatin, sirolimus, cyclophosphamide, and methyldopa are potential drugs for SARS-CoV-2 treatment. They also identified 10 microRNAs which are significant in treating SARS-CoV-2 disease.

## Vaccines

- This cohort study in Qatar aimed to assess protection from SARS-CoV-2 breakthrough infection after mRNA vaccination among persons with vs without prior SARS-CoV-2 infection. The study involved a total of 1,531,736 mRNA-vaccinated individuals between 21st December 2020 and 19th September 2021. The authors found that prior SARS-CoV-2 infection was associated with a statistically significant reduced hazard of breakthrough infection among recipients of both the BNT162b2 (adjusted hazard ratio, 0.62) and the mRNA-1273 (adjusted hazard ratio, 0.40).
- This study aimed to evaluate the effectiveness of the Johnson & Johnson Ad26.COV2.S vaccine for preventing SARS-CoV-2 infection. The comparative effectiveness research study used large-scale longitudinal curation of electronic health records from the multistate Mayo Clinic Health System U.S. to identify vaccinated (n=8889) and unvaccinated (n=88,898) adults between 27th February and 22nd July 2021. The authors found that Ad26.COV2.S vaccine had an effectiveness of 73.6% (95% CI, 65.9%-79.9%) and a 3.73-fold reduction in SARS-CoV-2 infections. Their findings suggest that a single dose of the Ad26.COV2.S vaccine appears highly effective at preventing SARS-CoV-2 infection even with the spread of variants such as Alpha or Delta, and reaffirm the urgent need to continue mass vaccination efforts globally.
- This phase 1, dose-finding study and an ongoing phase 2–3 randomised trial conducted in the U.S aimed to investigate the safety, immunogenicity, and efficacy of two doses of the BNT162b2 vaccine administered 21 days apart in children 6 months to 11 years of age. The authors present results for 5-to-11-year-old children. They found that two 10-µg doses of the BNT162b2 vaccine administered 21 days apart were safe, immunogenic, and 90.7% effective against COVID-19 in 5-to-11-year-old children. Their findings support vaccination of 5-to-11-year-old children with two 10-µg doses of the BNT162b2 vaccine.
- 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, Germany 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 cohort study aimed to assess antispike (anti-S) IgG antibody titres before and after a third BNT162b2 dose in individuals aged 60 years and older. The study involved 97 participants at the Rabin Medical Centre in Israel. The authors found that the median titre level increased significantly after the third dose, from a median of 440 AU/mL (IQR, 294-923) to 25 468 AU/mL (IQR, 14 203-36 618). There were no major adverse events reported.
- This retrospective cohort study utilised the electronic data bases of the largest health organisation (Clalit Health Services) in Israel to assess the association between vaccination with the BNT162b2 mRNA COVID-19 vaccine and Bell's palsy. A total of 132 cases of Bell's palsy were reported in 2,594,990 vaccinees with the first dose, and 152 cases in 2,434,674 vaccinees after the second dose. Their findings suggest that the mRNA COVID-19 vaccine might be associated with increased risk of Bell's palsy, and that this association appears to be more pronounced in older females after the first vaccine dose. The small estimated attributable risks suggest that the impact on public health is minor. They recommend further studies to examine this association especially in patients with previous history of Bell's palsy.
- This open label, prospective, non-randomised phase 1/2 trial aimed to assess safety, tolerability, and immunogenicity of Ad26-vectored COVID-19 candidate vaccine ("Sputnik Light") in a single centre in Russia. The study enrolled 110 participants. Their results show that the vaccine was well tolerated and produced both humoral and cellular immune responses in both seronegative and seropositive healthy adults. Single immunization of naïve volunteers is sufficient for rapid induction of immune responses against SARS-CoV-2 (100% seroconversion rate reached by day 42). Interestingly, "Sputnik Light" swiftly induced (by day 10) a more prominent immune response in the seropositive group of volunteers compared to the seronegative as well as the convalescents.
- This cross-sectional study applied a behavioural lens to understand drivers of COVID-19 vaccination uptake among healthcare workers (HCWs) in Nigeria. The authors found that about one-third of HCWs reported having gotten two doses of a COVID-19 vaccine. Motivation and ability were powerful predictors of vaccine uptake, with HCWs who had high motivation and high ability having a 15-times higher odds ratio of being fully vaccinated. However, only 27% of HCWs had high motivation and high ability. About 5% of HCWs had high ability but low motivation. This was primarily because the ability to get vaccinated was quite low among HCWs. Their findings highlight the urgency of making it easier for HCWs to get COVID-19 vaccinations.
- This cohort study aimed to assess whether the pragmatic application of the 3 COVID-19 vaccines (rAd26-rAd5, ChAdOx1, and BBIBP-CorV) available in Argentina were associated with a reduction in morbidity, all-cause mortality, and mortality due to COVID-19 in a population of individuals aged at least 60 years. The study involved 663,602 participants. The authors found that within the first 5 months after the start of the vaccination campaign, vaccination was associated with a significant reduction in COVID-19 infection as well as a reduction in mortality. Their results suggest the need to implement mass vaccination strategies with the vaccines that each country has available in the shortest possible time.
- This phase 1, dose escalation, open-label trial describes a COVID-19 vaccine based on a replication-defective gorilla adenovirus expressing the stabilized pre-fusion SARS-CoV-2 spike protein, named GRAd-COV2. The authors assessed the safety and immunogenicity of a single-dose regimen of this vaccine in healthy younger and older adults in Italy. Their findings provide evidence that GRAd-COV2 is well-tolerated in both younger and older age cohorts at all three doses assessed. The vaccine induced humoral and cellular responses to SARS-CoV-2 spike antigen similarly in younger and older adults. GRAd-COV2 merits further consideration as a SARS-CoV-2 vaccine candidate.
- This study estimated the role of waning immunity in the observed breakthrough against the delta variant in Israel. The authors used data on confirmed infection and severe disease collected from an Israeli national database for the period of 11th to 31st July 2021, for all residents who had been fully vaccinated before June 2021. Their findings indicate that immunity against the delta variant of SARS-CoV-2 waned in all age groups a few months after receipt of the second dose of vaccine. Their results provided an epidemiologic basis for the decision by the Israeli Ministry of Health to approve the administration of a

booster (third dose) of COVID-19 vaccine to persons who had been vaccinated at least 5 months previously.

- The authors in these in vitro and in vivo animal model studies in Canada produced and evaluated a novel protein subunit vaccine formulation containing a resistin-trimerized spike antigen, SmT1. Their vaccine induced robust antigen-specific humoral and cellular immune responses in mice. Antibodies had strong neutralising activity, preventing viral spike binding and viral infection. The formulations were highly efficacious in a hamster challenge model reducing viral load and body weight loss even after a single vaccination. The antigen-specific antibodies generated by their vaccine formulations had stronger neutralising activity than human convalescent plasma, neutralising the spike proteins of the B.1.1.7 and B.1.351 variants of concern.

## Diagnostics

- This practice review discusses relative merits and test characteristics of various commercially available technologies for SARS-CoV-2 testing. The review is written by members of the UK's COVID-19 National Diagnostic Research and Evaluation programme. They recommend further evaluations to verify the performance of the tests in COVID-19 variants and making the point-of-care tests more robust to detect new variants by targeting more than one SARS-CoV-2 gene or antigen.
- This modelling study in China compared the efficiency, accuracy, and cost of different screening methods during the COVID-19 pandemic. Their results show that PCR-based pooled screening is cost-effective in reversing the pandemic at low prevalence. When the prevalence is high, PCR-based pooled screening may not stop the outbreak. In contrast, antigen screening with sufficient frequency could reverse the epidemic, despite the high cost and the large numbers of false positives in the screening process.
- The authors in this study developed a two steps end point RT-PCR reaction with SARS-CoV-2 Nucleocapsid (N) gene and Ribonuclease P (RNase P) specific primers where viral amplicons were verified by agarose gel electrophoresis. They carried out a clinical performance and analytical sensitivity evaluation for the two-steps end point RT-PCR method with 242 nasopharyngeal samples obtained in Ecuador using the CDC RT-qPCR protocol as a gold standard technique. They observed a specificity of 95.8%, a sensitivity of 95.1%, and a limit of detection of 20 viral RNA copies/uL. Their proposed method is affordable and reliable for SARS-CoV-2 detection. Their protocol would allow to extend COVID-19 diagnosis to basic molecular biology laboratories with a potential positive impact in surveillance programs in developing countries.

## Care and Treatment

- This study reports the discovery and characterisation of PF-07321332 (Pfizer), an orally bioavailable SARS-CoV-2 main protease inhibitor with in vitro pan-human coronavirus antiviral activity and excellent off-target selectivity and in vivo safety profiles. PF-07321332 has demonstrated oral activity in a mouse-adapted SARS-CoV-2 model and has achieved oral plasma concentrations exceeding the in vitro antiviral cell potency in a phase I clinical trial in healthy human participants.
- This prospective cohort study aimed to describe the first 220 cases of definite or probable vaccine-induced immune thrombocytopenia and thrombosis (VITT) reported in the United Kingdom. Their results show that the condition often affects young, otherwise healthy vaccine recipients and manifests usually 5 to 30 days after the first vaccination with ChAdOx1 nCoV-19. The authors did not find any individual risk factors for VITT, but found increased mortality among patients who presented with severe thrombocytopenia, cerebral venous sinus thrombosis, intracranial haemorrhage, laboratory markers of severe coagulation activation, or all these variables. Treatment of the condition remains uncertain, but identification of prognostic markers may help guide effective management.
- This observational cohort study aimed to assess the prevalence and clinical implications of persistent or exertional cardiopulmonary symptoms in 3597 young competitive collegiate athletes following SARS-CoV-2 infection in the U.S. The authors found that both the prevalence of persistent symptoms from initial illness (1.2%) and exertional symptoms on return to exercise (4.0%) were low. No athlete with isolated persistent symptoms was diagnosed with SARS-CoV-2-associated clinical sequelae. In

athletes with exertional chest pain on return to exercise who underwent cardiac MRI (n=24), probable or definite SARS CoV-2 cardiac involvement was found in 20.8% of cases. Thus, a comprehensive symptom-guided evaluation is warranted in athletes with cardiopulmonary symptoms on return to exercise.

- This ongoing, double-blind, phase 3 trial at 37 sites in four countries (the United States, Canada, Brazil, and Spain) aimed to evaluate the efficacy and safety of sotrovimab in high-risk, ambulatory patients with mild-to-moderate COVID-19. Their findings showed that the relative risk reduction in hospitalisation (for >24 hours) or death between patients who received a single 500-mg dose of sotrovimab and those who received placebo was 85%. The authors did not identify any safety signals. Their findings indicate that sotrovimab can be a therapeutic agent for outpatients with COVID-19, they speculate that it has the potential to remain therapeutically active even as SARS-CoV-2 continues to evolve.
- This study characterises the anti-SARS-CoV-2 efficacy of GS-621763, an oral prodrug of remdesivir parent nucleoside GS-441524. Both GS-621763 and GS-441524 inhibit SARS-CoV-2, including variants of concern (VOC) in cell culture and human airway epithelium organoids. Twice-daily oral administration of 10 mg/kg GS-621763 reduces SARS-CoV-2 burden to near-undetectable levels in ferrets. Their results demonstrate therapeutic efficacy of a much-needed orally bioavailable analogue of remdesivir in a relevant animal model of SARS-CoV-2 infection.

## Epidemiology

- This retrospective cohort study in the United States aimed to compare characteristics, treatment, and outcomes of 80,449 patients with ST-segment elevation myocardial infarction (STEMI) with vs without COVID-19 infection. The authors found that the rates of in-hospital mortality for patients with vs without a concomitant diagnosis of COVID-19 were 15.2% vs 11.2% among those with out-of-hospital STEMI and 78.5% vs 46.1% among those with in-hospital STEMI; both differences were statistically significant. They recommend further research to understand the potential mechanisms underlying this association.
- This retrospective cohort study aimed to examine the impact of the Delta variant and vaccination among known index case-contact pairs in households to determine the secondary attack rates and risk factors for COVID-19 transmission. The study involved 1024 household contacts that were linked to 301 PCR confirmed index cases in Singapore between 1st September 2020 and 31st May 2021. Their results show that individuals exposed to the Delta variant have an increased risk of SARS-CoV-2 acquisition compared to those exposed to other variants. This risk was reduced by 55% among vaccinated individuals. Their findings suggest that vaccinated cases remain at risk of onward transmission of SARS-CoV-2 Delta variant, and therefore it is important to continue to contain spread through testing and isolation, and public health measures to prevent widespread community transmission.
- This cross-sectional study aimed to estimate the seroprevalence of SARS-CoV-2 antibodies in healthcare workers (HCWs) from 65 hospitals in 10 cities of Colombia during the second semester of 2020. The authors observed a seroprevalence rate of SARS-CoV-2 of 35% (95% Bayesian CI 33% to 37%) in HCWs, one of the higher ratios reported worldwide. The seroprevalence varied in the Colombian cities from 21% to 71%. Even though all the personnel reported the use of protective equipment, the seroprevalence in the general services personnel and nurses was high.
- This cohort study in Spain aimed to describe thrombotic complications among children infected with SARS-CoV-2 across 49 hospitals. The authors found that 4 patients out of 537 infected children developed a thrombotic complication. D-dimer value was not specific enough to predict thrombotic complications. Adolescence and previous thrombotic risk factors may be considered when initiating anticoagulant prophylaxis in children with COVID-19. They recommend further studies to clarify risk factors among children with COVID-19 in order to develop specific recommendations.
- This study assessed RT-PCR swab-positivity in the REal-time Assessment of Community Transmission-1 (REACT-1) study in England. The authors observed sustained exponential growth with average doubling time (June-July 2021) of 25 days driven by complete replacement of Alpha variant by Delta, and by high prevalence at younger less-vaccinated ages. Unvaccinated people were three times more likely than double-vaccinated people to test positive. However, after adjusting for age and

other variables, vaccine effectiveness for double-vaccinated people was estimated at between ~50% and ~60% during this period in England. Increased social mixing in the presence of Delta had the potential to generate sustained growth in infections, even at high levels of vaccination.

- This population-based survey on the southern coast of Kenya aimed to assess whether differences existed in social contact patterns between different contexts and how these differences affected age-specific social mixing. Their results provide a robust comparison of social mixing patterns across diverse demographic settings along the rural–urban gradient, and identify which individuals' profiles, based on their age mixing patterns and daily time use behaviour. These findings could be instrumental in defining effective interventions that acknowledge the heterogeneity in social contexts and daily routines, either in Kenya or other demographically and culturally similar sub-Saharan African settings.

### Infection Prevention and Control

- This multicentre, pragmatic open-label, parallel, cluster-randomised trial aimed to evaluate a 5-day course of Lopinavir/ritonavir (LPV/r) post-exposure prophylaxis (PEP) among asymptomatic individuals with documented exposure to SARS-CoV-2 in Brazil and Switzerland. Their trial was inconclusive and produced only weak evidence in favour of LPV/r as prophylactic treatment for persons in close contact with SARS-CoV-2. They recommend additional trials to strengthen the evidence for or against this prophylactic option.
- This prospective observational study aimed to measure air and surface environmental contamination with SARS-CoV-2 virus when high-flow nasal oxygen (HFNO) and continuous positive airway pressure (CPAP) are used, compared with supplemental oxygen, to investigate the potential risks of viral transmission to healthcare workers and patients. The study was conducted across 3 UK hospitals. The authors found that the use of CPAP and HFNO to treat moderate/severe COVID-19 did not appear to be associated with substantially higher levels of air or surface viral contamination in the immediate care environment, compared with the use of supplemental oxygen. Their findings add to the increasing evidence that for COVID-19, CPAP and HFNO may not be procedures with a higher transmission risk that are associated with their 'aerosol generating' classification. Rather, healthcare worker exposure and nosocomial transmission may be more influenced by patient factors, such as coughing at earlier stages of infection, than the type of respiratory support used.
- This prospective observational study aimed to characterise aerosol emission from high-flow nasal oxygen (HFNO) and continuous positive airway pressure (CPAP) and compare with breathing, speaking and coughing. The study recruited healthy volunteers in the UK to breathe, speak and cough in ultra-clean, laminar flow theatres followed by using CPAP and HFNO. The authors used 2 discrete methodologies simultaneously to measure aerosol emission. Hospitalised patients with COVID-19 had cough recorded using the same methodology on the infectious diseases ward. Their results suggest that risk of SARS-CoV-2 infection is not due to CPAP or HFNO generating infective aerosols. This has implications for infection and prevention control policy since aerosol generation appears greatest from patients with COVID-19 who are coughing.

### Non-pharmaceutical interventions, social distancing

- This modelling study aimed to estimate the cost-effectiveness of implementing a national Test-Trace-Isolate (TTI) program to reduce the number of severe and fatal cases of COVID-19 in Colombia. The authors found that, compared with no intervention, the TTI program saves an average of $1,045 and $850 per case when observed from the social and the health system perspective, respectively. TTI reduces the demand for highly specialised medical services (ICU hospitalisation days) and the mortality rate. Their findings are significantly important for both Low- and Middle- Income countries where the budget is highly limited and High-Income countries where the COVID-19 vaccination rate is under the herd immunity level.
- This national online-survey in Canada aimed to characterise self-reported non-adopters of non-pharmaceutical interventions (NPIs) compared to people who reported following these behaviours. The survey involved 4498 respondents. Their findings revealed that: (1) being male, (2) age 18–34 years, (3) Albertans, (4) lower education level, and 5) a higher conservative political leaning were associated

with non-adoption of NPIs. Participants who expressed low concern for COVID-19 had greater odds of being non-adopters. Non-adoption was associated with greater distrust among several institutions including technology, professional services, healthcare and government. Respondents who reported that public health messaging has been unclear and inconsistent and those where messaging has made them less likely to adopt NPIs had greater odds of non-adoption. Their findings are important to inform targeted marketing interventions.

## D. Clinical Trials Updates

**Key updates:**

Vaccine trials:

- On 5th November 2021, Ocugen with its partner Bharat Biotech announced it has submitted a request to the U.S. Food and Drug Administration (FDA) for Emergency Use Authorization (EUA) of its COVID-19 vaccine candidate, COVAXIN (BBV152) for children between 2 to 18 years. Coaxin is a whole-virion, inactivated vaccine manufactured using a Vero Cell manufacturing platform as has been used in the production of inactivated polio vaccine. The submission was based on the results of 526 participants aged 2 to 18 years from an open-label, multicentre phase 2/3 paediatric clinical trial which enrolled 526 participants aged 2 to 18 years in India. According to the data, neutralizing antibody responses against wild-type strain in the paediatric age group of 2-18 years were equivalent to those seen in adults, aged 18+ years, in the company's large phase 3 efficacy and safety trial. More than 90 percent of the seroconversion rates were observed for antibody titres against S1, RBD, N proteins and wild-type neutralizing antibodies. Furthermore, no serious adverse events or hospitalizations were observed in phase 2/3 paediatric study including no events of special interest such as Guillain-Barre Syndrome, anaphylactic reactions, myocarditis, pericarditis, and vaccine-induced thrombotic thrombocytopenia. These results suggest similar protection in children, ages 2-18, to that demonstrated in adults older than 18 years. Clinical trial registration #: NCT04918797
- On 3rd November 2021, World Health Organization (WHO) issued an Emergency Use Listing for Covaxin COVID-19 vaccine for use in individuals aged >18 years. Covaxin was assessed under the WHO EUL procedure based on the review of data on quality, safety, efficacy, a risk management plan and programmatic suitability. The WHO Technical Advisory Group (TAG) has determined that the vaccine meets WHO standards for protection against COVID-19 and that the benefit of the vaccine far outweighs risks and the vaccine can be used globally. With validation from the WHO, countries can now expedite their regulatory approval processes to import and administer COVAXIN vaccine. In addition, UNICEF, Pan-American Health Organization (PAHO), GAVI COVAX facility, can procure Covaxin vaccine for global distribution.
- On 27th October 2021, Ocugen announced that it has submitted an investigational new drug (IND) application to the US Food and Drug Administration (FDA) requesting for approval to initiate a phase 3 clinical trial of its COVID-19 vaccine candidate, Covaxin (BBV152). The company plans to recruit more than one hundred healthy adults in the U.S into the phase 3 immuno-bridging study, OCU-002, upon obtaining the FDA approval. The participants of the study should include those that have either not been vaccinated or have received two doses of a messenger ribonucleic acid (mRNA) shot at least six months earlier. They will be categorized to receive either two doses of Covaxin or placebo, 28 days apart. The trial's primary endpoint is to compare blood-based samples taken from U.S. participants who received Covaxin against samples of the participants in the phase 3 efficacy trial conducted in India. The secondary endpoint will involve testing the immunogenic profile of the vaccine. The study will also assess the safety and tolerability of the Covaxin in the U.S. population. Clinical trial registration #: NCT04641481

Therapeutics trials:

- On 9th November 2021, Inovio announced that the U.S. Food and Drug Administration (FDA) has granted authorization to advance subjects enrolment into phase 3 segment of its global INNOVATE clinical trial for its COVID-19 vaccine candidate, INO-4800, in the United States. The phase 3 segment of the INNOVATE clinical trial aims to evaluate the efficacy of INO-4800 in a two-dose regimen (2.0 mg per dose) administered one month apart. The trial will enrol adult subjects aged ≥18 years and randomize them in a 2:1 ratio. The primary endpoint of phase 3 INNOVATE clinical trial is virologically confirmed symptomatic COVID-19. INOVIO is working with Advaccine Biopharmaceuticals Suzhou Company to conduct the phase 3 segment of the INNOVATE trial in multiple countries including the Americas, Asia, and Africa. Currently, the company has received authorization to conduct phase 3 segment of the INNOVATE clinical trial in the United States, India, Brazil, Philippines, Mexico, Colombia, and Thailand. Clinical trial registration #: NCT04642638
- On 5th November 2021, Pfizer reported positive initial results of the phase 2/3 EPIC-HR clinical trials for its investigational novel COVID-19 oral antiviral candidate, PAXLOVID, for the treatment of COVID-19 patients. Paxlovid is an experimental inhibitor of SARS-CoV-2-3CL protease, an enzyme required by the coronavirus for replication. This randomised, double-blinded phase 2EPIC-HR clinical trial enrolled non-hospitalized COVID-19 patients, who were at high risk of progressing to severe illness. According to the data from 1, 219 subjects enrolled, PAXLOVID was found to reduce the risk of hospitalization or death by 89% compared to placebo and 0.8% of the subjects in the Paxlovid arm were admitted to the hospital by day 28 as against 7% in the placebo group who were hospitalised or died. No deaths were reported in patients who received PAXLOVID as compared to 10 deaths in patients who received placebo. Pfizer plans to submit the data as part of its ongoing rolling submission to the U.S. FDA for Emergency Use Authorization (EUA) as soon as possible.
- On 4th November 2021, Merck and Ridgeback Biotherapeutics announced that the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) has approved molnupiravir drug for the treatment of mild-to-moderate COVID-19 adult patients in the United Kingdom. The decision is based on the positive results from phase 3 MOVe-OUT clinical trial which showed that molnupiravir reduced the risk of hospitalisation or death by almost 50%. Molnupiravir is an investigational, orally administered form of a potent ribonucleoside analogue that inhibits the replication of SARS-CoV-2. Merck has filed for emergency approval for molnupiravir in the US and Canada. European Medicines Agency has initiated a rolling review of the antiviral drug. Merck is committed to increase supply and provide timely access to molnupiravir globally. Molnupiravir has become the first oral antiviral medicine authorized for the treatment of mild-to-moderate COVID-19 in adults with a positive SARS-CoV-2 diagnostic test.
- On 4th November 2021, NRx Pharmaceuticals announced that the United States Food and Drug Administration (FDA) has declined to issue an Emergency Use Authorization (EUA) for ZYESAMI (aviptadil) to treat critical COVID-19 patients who have respiratory failure. The decision came due to insufficient data regarding the known and potential benefits and risks of ZYESAMI in treating critical COVID-19 patients with respiratory failure. FDA has so far reviewed safety data in only 131 randomised patients treated with ZYESAMI. However, NRx will work with FDA to review 150 or more additional patients already treated with ZYESAMI in the NIH ACTIV-3b trial. The Data Safety and Monitoring Board of the NIH ACTIV-3b trial reviewed data and found no new safety issues related to the ZYESAMI treatment. The company has sought a Type A meeting with FDA authorities to discuss the experimental treatment's development. ZYESAMI clinical trials which are funded by the US National Institutes of Health and BARDA continue and advance towards enrolment in Brazil and Europe.
- On 3rd November 2021, Resverlogix announced that it is in discussion with the Ministry of Health of the Kingdom of Morocco to conduct phase II clinical trials of its drug, apabetalone (RVX-208), for COVID-19. Apabetalone (RVX-208), is an epigenetic small molecule or gene regulating therapeutic candidate which selectively inhibit BET (Bromodomain and Extra-Terminal). It works in preventing disease by switching genes on and/or off through regulation of gene expression. Phase II clinical trials of

apabetalone (RVX-208) are currently planned to enrol up to 100 confirmed COVID-19 patients in Canada and Brazil. Subjects will either receive twice daily doses of apabetalone for up to 4 weeks alongside standard of care, or standard of care alone. The primary outcome measure of the study will be a change in the World Health Organization (WHO) Ordinal Scale for Clinical Improvement. Clinical trial registration #: NCT04894266

- On 2nd November 2021, NRx Pharmaceuticals reported that its experimental drug, Zyesami (aviptadil), was found to be safe to treat COVID-19 in the Phase III ACTIV-3b Critical Care clinical trial sponsored by the US National Institutes of Health (NIH). The Independent Data Safety Monitoring Board of the trial recommended continuation of the subject enrolment after review of data from more than 300 patients found no new safety concerns. This placebo-controlled randomised ACTIV-3b clinical trial is testing ZYESAMI and remdesivir (Veklury) as separate single agent and in combination in hospitalized COVID-19 patients with acute respiratory failure who require high-flow supplemental oxygen delivered by nasal cannula, mechanical ventilation, or extracorporeal membrane oxygenation. The company has submitted a request for Emergency Use Authorization to the US Food and Drug Administration (FDA) for ZYESAMI for the treatment of patients suffering from Critical COVID-19 with respiratory failure since May 2021.
- On 27th October 2021, Sorrento Therapeutics reported positive interim results from two Phase 2 studies of its oral drug, Abivertinib, for the treatment of hospitalized severe COVID-19 patients. Abivertinib is an oral capsule that potentially reduces cytokine storm associated with acute respiratory distress syndrome (ARDS) in severely hospitalized COVID-19 patients. The two randomised, double-blinded phase 2 clinical trials assessed the safety and efficacy of Abivertinib drug in hospitalized Covid-19- patients with pneumonia and respiratory depression. The trials recruited up to 96 subjects in the United States and 400 subjects in Brazil. Initial results from two phase 2 studies showed improvement of at-risk COVID-19 patients in avoiding death and respiratory failure at one month (20% improvement in the US study [78.3% vs. 58.3%] and 25% in the Brazil study [69.6% vs. 44.4%], respectively for Abivertinib vs. controls). Also, at-risk patients in the US were discharged on average 2 days sooner from the ICU. Abivertinib has the potential to fill the unmet need for the at-risk COVID-19 patients and significantly reduce progression to intubation, mechanical ventilation and death. Clinical trial registration #: NCT04440007
- On 26th November 2021, Vaxart reported that it has begun dosing the first subject in its phase 2 clinical trial of an oral COVID-19 tablet for the treatment of COVID-19 patients in the United States. The US part of the phase 2 clinical trial is an open-label, randomised dose and age escalation lead-in segment in untreated and previously inoculated participants. The study is designed to enrol 96 subjects aged 18 to 75 years. Subjects will be grouped into eight strata based on their age, inoculation history, and dosage size to receive either the oral tablet vaccine or placebo on day one and day 29. The study's endpoints are safety, immunogenicity and efficacy of the COVID-19 oral tablet. A global placebo-controlled efficacy trial which will recruit a larger pool of subjects is anticipated to be initiated after the US trial is completed. Clinical trial registration #: NCT 05067933
- On 26th October 2021, Axcella Therapeutics announced the launching of a new clinical program to investigate its drug therapy, AXA1125 as a potential treatment for Long COVID-19. Long COVID is also known as post-COVID-19 and post-acute sequelae of COVID-19 (PASC). This decision came after the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom accepted the clinical trial authorisation submission for a phase 2a trial for AXA1125. This randomised, double-blind, placebo-controlled phase 2 trial will assess the efficacy and safety of AXA1125 in patients with exertional fatigue related to Long COVID. The trials will recruit up to 40 participants who will be categorized equally to receive either 67.8g AXA1125 drug or a matched placebo daily for 28 days. The trial is planned to begin at the Oxford Centre for Clinical Magnetic Resonance Research.

Immunotherapies trials:

- On 8th November 2021, Regeneron Pharmaceuticals announced positive additional results from a phase 3 clinical trial of a single dose of its experimental therapy, REGEN-COV, for prevention of COVID-19 in uninfected people. REGEN-COV is a cocktail of two monoclonal antibodies, casirivimab and imdevimab, designed to prevent COVID-19 infectivity. This randomised, placebo-controlled, double-blind phase 3 clinical trial enrolled uninfected people from the household of a COVID-19 infected person. Participants were categorized into 1:1 to receive either a 1,200mg dose of REGEN-COV, administered as four subcutaneous injections, or a placebo. According to the analysis of data from 1,683 new subjects, a single dose of REGEN-COV was found to reduce risk of COVID-19 infection by 81.6% during the pre-specified follow-up period of two to eight months. The new results are consistent with the results of the previous report which showed that REGEN-COV reduced the risk of COVID-19 by 81.4% in people exposed to SARS-COV-2. In addition, during the 8-month assessment period there were no hospitalizations for COVID-19 in the REGEN-COV group compared to 6 in the placebo group. Clinical trial registration #: NCT04425629

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

## Contributors

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