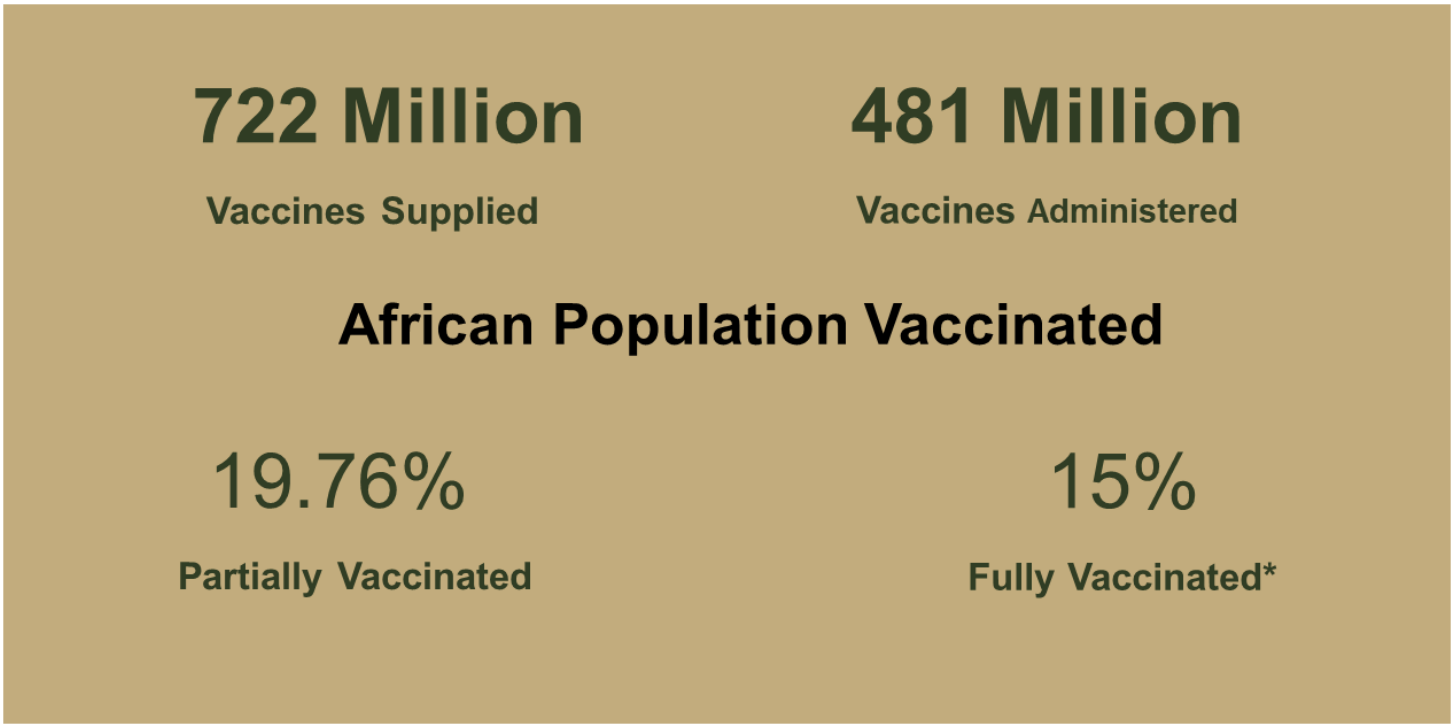
COVID-19 Scientific and Public Health Policy Update[1]

(16 March 2022)

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, this biweekly brief details the latest developments in scientific knowledge and public health policy from around the world as well as updates to the COVID-19-related guidance from Africa CDC, WHO and other public health agencies. Contents of this brief are ***not intended to serve as recommendations*** *from the African Union-Africa CDC or WHO/AFRO; rather, the brief serves as 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 on the science and public health best practices related to COVID-19.*

A. Trending Topics

Status of Vaccines in Africa

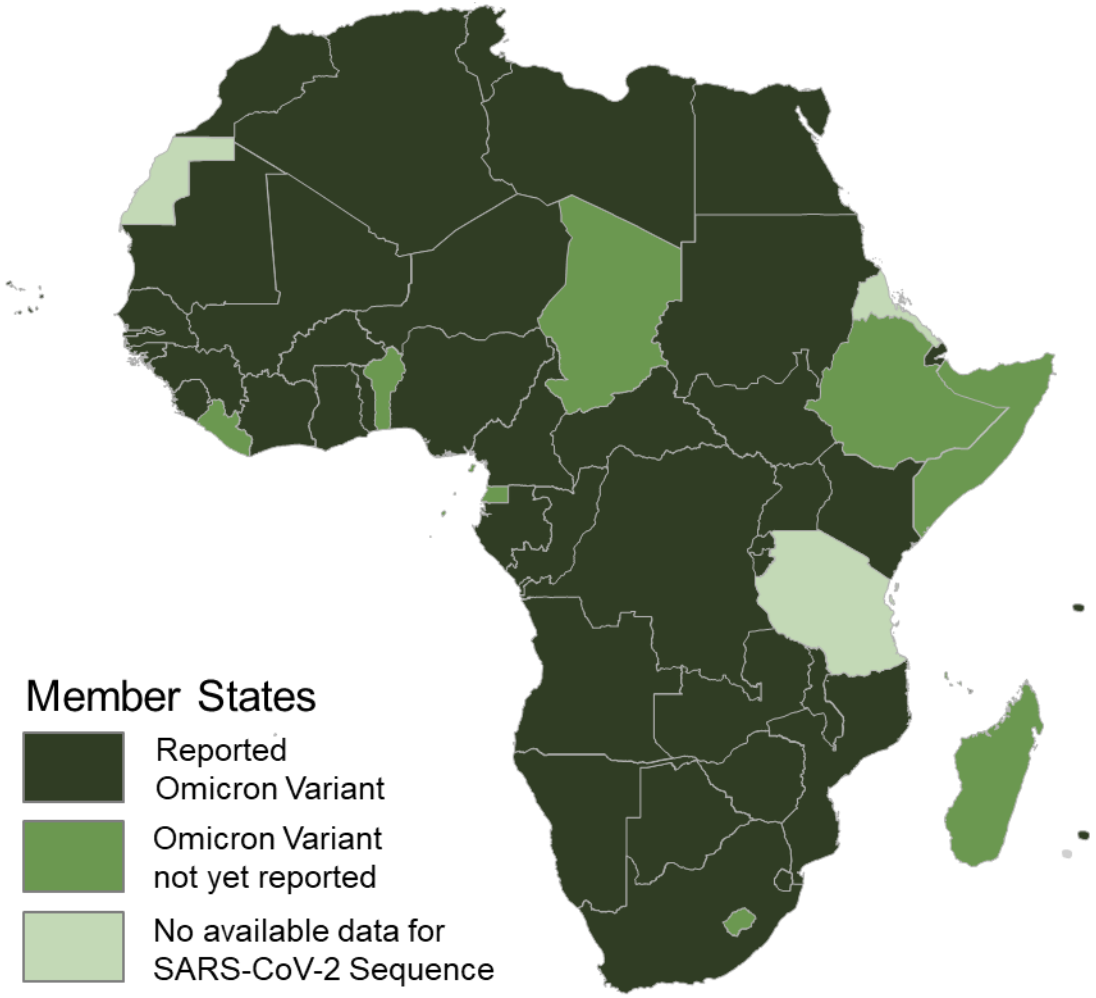


*Received two doses of a two dose COVID-19 vaccine series or one dose of the Johnson & Johnson vaccine
https://africacdc.org/COVID-19-vaccination/
Updated 16th March, 2022

[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 does not represent policy decisions, recommendations, or final conclusions of the African Union- Africa CDC or WHO/AFRO**.

Variants of Concern (VOC)

The Omicron variant (B.1.1.529), first reported in South Africa on 24th November 2021, has spread to 196 countries/territories/areas worldwide. As of 16 March 2022, 43 (78.2%) of the 55 Member States in Africa have reported this variant. For more information visit https://africacdc.org/institutes/africa-pathogen-genomics-initiative/.



Updated 16th March, 2022

B. New guidelines and resources

Since 2nd March 2022,

- Africa CDC[2] has published new guidance and resources on:
  - Outbreak Brief 112: Coronavirus Disease 2019 (COVID-19) Pandemic

- U.S. CDC[3] has published new guidance and resources on:
  - Interim Guidance for Rapid Antigen Testing for SARS-CoV-2
  - Operational Considerations for Immunisation Services during COVID-19 in Non-US Settings Focusing on Low-Middle Income Countries
  - Guidance for General Laboratory Safety Practices during the COVID-19 Pandemic

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

- WHO[4] has published new guidance and resources on:
  - Annexes to the interim recommendations for use of theChAdOx1-S [recombinant] vaccine against COVID-19
  - Strengthening COVID-19 vaccine demand and uptake in refugees and migrants
  - Virtual cGMP Training Marathon for Vaccine Manufacturing: Questions & Answers
  - Safety monitoring of molnupiravir for treatment of mild to moderate COVID-19 infection in low and middle-income countries using cohort event monitoring: a WHO study
  - Use of SARS-CoV-2 antigen-detection rapid diagnostic tests for COVID-19 self-testing
  - Infection prevention and control in the context of coronavirus disease (COVID-19): A living guideline

- U.S. FDA[5] has issued press releases on:
  - On 4th March, the FDA authorised an extension for the shelf life of the refrigerated Janssen COVID-19 Vaccine, from six to nine months, allowing the product to be stored at 2-8 degrees Celsius
  - As of 15th March, 422 tests and sample collection devices are authorised by the FDA under emergency use authorisations

- ECDC[6] has issued new resources on:
  - Analysis of COVID-19 contact tracing data from Ireland, Italy and Spain – 2020 data
  - Interim analysis of COVID-19 vaccine effectiveness against Severe Acute Respiratory Infection due to laboratory-confirmed SARS-CoV-2 among individuals aged 30 years and older, ECDC multi-country study – second update
  - Operational public health considerations for the prevention and control of infectious diseases in the context of Russia's aggression towards Ukraine

- UKHSA[7] has issued new guidance and press releases on:
  - COVID-19: infection prevention and control (IPC)
  - Guidance for care of the deceased with suspected or confirmed coronavirus (COVID-19)
  - Assessment and procurement of coronavirus (COVID-19) tests
  - COVID-19 rapid lateral flow test kit instructions: throat and nose test
  - PCR home testing for people eligible for new COVID-19 treatments
  - COVID-19 serology and viral detection tests: technical validation reports

Scientific updates

Basic Science

- This case-control study in the United Kingdom compared genomes from 7,491 critically-ill cases with 48,400 population controls in order to find underlying disease mechanisms. The authors used whole genome sequencing and discovered 23 independent variants that significantly predispose to critical Covid-19. They identified 16 new independent associations, including variants within genes involved in interferon signalling (*IL10RB*, *PLSCR1*), leucocyte differentiation (*BCL11A*), and blood type antigen secretor status (*FUT2*). They also found evidence implicating multiple genes, including reduced expression of a membrane flippase (*ATP11A*), and increased mucin expression (*MUC1*), in critical disease. Mendelian randomisation provided evidence in support of causal roles for myeloid cell adhesion molecules (*SELE*, *ICAM5*, *CD209*) and coagulation factor *F8*, all of which are potentially druggable targets. Their results are broadly consistent with a multi-component model of Covid-19 pathophysiology, in which at least two distinct mechanisms can predispose to life-threatening disease:

[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] UKHSA: United Kingdom Health Security Agency

failure to control viral replication, or an enhanced tendency towards pulmonary inflammation and intravascular coagulation.

- This case report from Brazil presents the first case of intra-host SARS-CoV-2 recombination during a coinfection by the variants of concern (VOC) AY.33 (Delta) and P.1 (Gamma). The authors performed next generation sequencing on a nasopharyngeal swab sample from a 32-year-old male with mild flu-like symptoms of fever, headache, cough, fatigue, and sore throat. They found sequencing reads intersecting regions that simultaneously overlap lineage-defining mutations from Gamma and Delta. They identified a total of 6 recombinant regions across the SARS-CoV-2 genome. Four of them mapped in the spike gene and two in the nucleocapsid gene. Their findings represent a possibility of the emergence of viruses with recombinant phenotypes that are a threat to public health management during the pandemic.
- This review describes how each of the COVID-19 vaccines, antibody therapies, and antiviral drugs that have been approved to date were built on decades of investment in technology and basic science. The review also describes the interactions of SARS-CoV-2 with the immune system and those therapies that target the host response to infection. The authors recommend steps that need to be taken now to prepare for, to minimise the effects of, and ideally to prevent future pandemics.
- This study reviews the results of almost 2 years of COVID-19 immunology research and discuss definitive findings and remaining questions regarding the understanding of COVID-19 pathophysiology. The authors also discuss emerging understanding of differences in immune responses seen in those with and without Long Covid Syndrome.

Vaccines

- This matched case-control study in the United States assessed the effectiveness of the BNT162b2 vaccine in adolescents aged 12 to 18 years. The study involved 542 adolescents (186 case and 356 matched control participants). Overall, 134 (25%) were fully immunised (case participants, 10 [5%]; control participants, 124 [35%]). The median time between immunisation and the SARS-CoV-2 test was 62 days (range, 17-129 days). Within 4 months of receiving 2 doses, the vaccine's effectiveness (VE) against any infection was estimated to be 91% (95% CI, 80%-96%); and against asymptomatic infection, 85% (95% CI, 57%-95%). Effectiveness after a single dose was estimated to be 74% (95% CI, 18%-92%). These findings suggest that the BNT162b2 vaccine was effective in adolescents within 4 months of immunisation, including against infections caused by the Delta variant.
- This prospective, longitudinal comparative effectiveness study in Switzerland assessed the humoral responses in immunocompromised patients and healthy controls after vaccination with BNT162b2 & mRNA-1273 vaccines. The study involved 637 immuno-compromised patients (399 with solid cancers, 101 with hematologic cancers, 38 with solid organ transplants & 99 with autoimmune diseases) and 204 healthy control participants who received 2 doses of messenger RNA COVID-19 vaccines. Neutralising antibody (nAb) responses against the Beta and Delta variants were short lived (3 to 7 months) compared with original, nonvariant SARS-CoV-2 and other variants. Approximately half of patients with hematologic cancers and solid cancers, about 70% of patients with solid organ transplants or autoimmune diseases, and 40% of healthy controls lost nAbs against the circulating VOCs at 6 months after vaccination. Higher nAb titers and longer durability of humoral responses were associated with vaccination with the mRNA-1273 vaccine. Their findings suggest that boosting vaccine strategies need to be personalised to the underlying disease.
- This retrospective cohort study in Taiwan assessed the adverse events following COVID-19 vaccination in patients with rheumatic diseases. The study enrolled 265 patients; with Sjogren's syndrome (n=49), rheumatoid arthritis (n=34), systemic lupus erythematosus (n=33), spondyloarthritis (n=21) and other rheumatic diseases. Eighty-nine (33.7%) patients received ChAdOx1 nCoV-19 (AZD1222) vaccine and 176 (66.3%) received mRNA-1273 vaccines. The overall adverse events were comparable in AZD1222 (18%) and mRNA-1273 groups (19%). The AZD1222 was associated with prolonged constitutional symptoms (6.7% vs 1.1%, p value=0.019), but the flare rates of rheumatic diseases (5.6% vs 6.2%) were similar in both groups. Notably, herpes zoster reactivation occurred in 10 patients among mRNA-1273 recepients versus no reactivation in the AZD1222 group (6.2% vs 0%,

p value=0.019). The median time from vaccination to herpes zoster attack was 10 days. Of note,, 9 patients experienced the first herpes zoster event in their lives and multidermatome involvement was seen in 5 patients. Two patients experienced complications with pemphigus-like oral mucositis and one patient developed toxic epidermal necrolysis (TEN).

- This retrospective cohort study in Hong Kong among 5493 patients with rheumatic arthritis assessed the relationship between COVID-19 full vaccination (two completed doses) and occurrence of arthritis flares. The patients received BNT162b2 (n=653); CoronaVac (n=671) and 4169 were not vaccinated. Propensity-scored weighted poisson regression showed no significant association between arthritis flare and COVID-19 vaccination (BNT162b2: adjusted incidence rate ratio 0.86(95% CI 0.73 to 1.01); CoronaVac: 0.87 (0.74 to 1.02)). The distribution of weekly rheumatic drug prescriptions showed no significant differences among the three groups since the launch of the mass vaccination programme (all p values >0.1). Real-world vaccine safety surveillance with direct disease activity testing related to arthritis flare should continue to provide more robust evidence on the
- This cross-sectional study in China assessed the risk of gout flares in the first 3 months after COVID-19 vaccination with inactivated virus vaccines. The study involved 549 gout patients of which 462 received a COVID-19 vaccine (250 (54.1%) received the Sinovac Life vaccine; 174 (37.7%) had the Sinopharm BIBP; and 38 (8.2%) the others (recombinant COVID-19 vaccine (CHO cell) or recombinant COVID-19 Vaccine (adenovirus type 5 vector)). A total of 203 patients (43.9%) developed at least one gout flare in the 3 months following vaccination. Most of the flares were experienced within 1 month after the first (99/119 (83.2%)) or second (70/115 (60.9%)) dose of the vaccine. Compared with unvaccinated participants, COVID-19 vaccination was associated with higher odds of gout flare within 3 months (adjusted OR 6.02; 95% CI 3.00 to 12.08). Colchicine use was associated with a 47% less likelihood of post-vaccine gout flare.

Diagnostics

- This diagnostic study in the United States assessed the use of rapid antigen testing at day 5 after exposure among asymptomatic quarantined school contacts of students with confirmed SARS-CoV-2 test results in 1 Florida county during a surge of cases attributed to the Delta variant. The study involved 603 asymptomatic student contacts. The contacts were tested by both rapid antigen tests and RT-PCR. Of the contacts tested, 25 (4.1%) had a positive rapid antigen test result (independent of RT-PCR test results), and 30 (5.0%) had a positive RT-PCR test result (independent of rapid antigen test results). Twenty-four (4.0%) had positive test results by both modalities. One contact (0.2%) had positive antigen and negative RT-PCR results; 6 (1.0%) had negative antigen and positive RT-PCR results, and 572 (94.9%) had negative results by both modalities. They found that rapid antigen testing had a sensitivity of 80.0% [95% CI, 61.4%-92.3%] and specificity of 99.8% [95% CI, 99.0%-100.0%]. The tests were highly concordant (Cohen κ, 0.87 [95% CI, 0.79-0.95]). The high congruence of the rapid antigen test with RT-PCR test may inform the recommendations to minimise student absenteeism owing to quarantine.

Care and Treatment

- This study reviewed the first 100 consecutive patients who received sotrovimab at health care facilities in Australia during the B.1.617.2 (delta) variant outbreak. The authors identified 8 patients that were persistently positive for SARS-CoV-2. Genomic analysis showed that 4 of the 8 patients acquired mutations in S:E340 within 6 to 13 days after they received sotrovimab. Cultures obtained from these patients remained positive for 23, 24, 12, and 15 days, respectively. Their findings show rapid development of spike gene mutations associated with high-level sotrovimab resistance in vitro. These findings underscore the importance of stewardship of monoclonal antibodies, particularly because sotrovimab is one of the few monoclonal antibodies with retained activity against the B.1.1.529 (omicron) variant.
- This randomised, controlled, open-label platform trial in the United Kingdom evaluated the use of baricitinib, a Janus kinase (JAK) 1/2 inhibitor, for the treatment of patients admitted to hospital because of COVID-19. The study involved 8156 patients across 159 hospitals. The patients were randomly

allocated (1:1) to receive usual care plus baricitinib (4 mg once daily by mouth for 10 days or until discharge if sooner) versus standard of care alone. Overall, 513 (12%) of 4148 patients allocated to baricitinib versus 546 (14%) of 4008 patients allocated to standard care died within 28 days (age-adjusted rate ratio 0.87; 95% CI 0.77-0.98; p=0.026). This 13% proportional reduction in mortality was somewhat smaller than that seen in a meta-analysis of 8 previous trials of a JAK inhibitor (involving 3732 patients and 425 deaths) in which allocation to a JAK inhibitor was associated with a 43% proportional reduction in mortality (rate ratio 0.57; 95% CI 0.45-0.72). The total randomised evidence to date suggests that JAK inhibitors (chiefly baricitinib) reduce mortality in patients hospitalised for COVID-19 by about one-fifth. [*not peer reviewed*]

- This retrospective cohort study at 15 medical centres in the United States assessed whether continuing dexamethasone treatment at discharge was associated with reduced all-cause readmissions or mortality post-discharge. The study included 1164 adults who received less than 10 days of dexamethasone (6 mg/d) until discharge during hospitalisation for COVID-19 and were discharged alive between 1 May and 30 September 2020. The authors found that the rate of readmission or mortality within 14 days of discharge was 9.1% among patients who continued dexamethasone treatment compared with 11.4% among patients who did not. This difference was not statistically significant. The findings suggest that dexamethasone should not be routinely prescribed beyond discharge for individuals with COVID-19.
- This retrospective cohort study in the United States analysed the mortality rate and complications associated with treatment of COVID-19 at dedicated COVID-19 hospitals. The study involved 5504 patients admitted in 11 hospitals in Minnesota, including 2 hospitals created solely to care for patients with COVID-19. Of these, 2077 patients (37.7%) were treated at 1 of the 2 COVID-19-dedicated hospitals. The mortality rate was 11.6% (n = 241) at the dedicated hospitals compared with 8.0% (n = 274) at the other hospitals ($P < .001$). However, risk-adjusted in-hospital mortality was significantly lower for patients in the COVID-19–dedicated hospitals in both the unmatched group (n = 2077; odds ratio [OR], 0.75; 95% CI, 0.59-0.95) and the propensity score–matched group (n = 1317; OR, 0.78; 95% CI, 0.58-0.99). The rate of overall complications in the propensity score–matched group was significantly lower (OR, 0.81; 95% CI, 0.66-0.99) and the use of COVID-19–specific therapeutics including deep vein thrombosis prophylaxis (83.9% vs 56.9%; $P < .001$), high-dose corticosteroids (56.1% vs 22.2%; $P < .001$), remdesivir (61.5% vs 44.5%; $P < .001$), and tocilizumab (7.9% vs 2.0; $P < .001$) was significantly higher. Their findings suggest that there is improved in-hospital mortality for patients treated at dedicated hospitals owing to improved processes of care.
- This systematic review and meta-analysis of 16 randomised trials summarises specific adverse effects of remdesivir, hydroxychloroquine and lopinavir/ritonavir in patients with COVID-19. This study directly informs the living WHO guideline for COVID-19 therapeutics. The authors found moderate certainty evidence that hydroxychloroquine increases the risk of diarrhoea and nausea and/or vomiting. They also found low certainty evidence that hydroxychloroquine increases the risk of cardiac toxicity (risk difference (RD) 10 more per 1000, 95% CI 0 more to 30 more) and cognitive dysfunction/delirium (RD 33 more per 1000, 95% CI 18 fewer to 84 more). For lopinavir/ritonavir, they found low certainty evidence that it increases the risk of diarrhoea (RD 168 more per 1000, 95% CI 58 more to 330 more), and nausea and/or vomiting (RD 160 more per 1000, 95% CI 100 more to 210 more). Based on low or very low certainty evidence, they did not find evidence that remdesivir or lopinavir/ritonavir increase the risk of acute kidney injury (RD 8 fewer per 1000, 95% CI 27 fewer to 21 more) or cognitive dysfunction/delirium (RD 3 more per 1000, 95% CI 12 fewer to 19 more).
- This randomised, double-blind, placebo-controlled, phase 3 study in the United States assessed the safety and therapeutic effect of CD24Fc (an immunomodulator with potential to reduce the exaggerated inflammatory response to tissue injuries) for hospitalised patients with COVID-19 who were receiving oxygen support. The study enroled 234 patients across 9 centres. The patients were assigned to receive a single intravenous infusion of CD24Fc 480 mg (n=116) or placebo (n=118). Median time to clinical improvement was 6·0 days (95% CI 5·0–9·0) in the CD24Fc group versus 10·5 days (7·0–15·0) in the placebo group (HR 1·40, 95% CI 1·02–1·92; log-rank p=0·037). The proportion of participants with disease progression within 28 days was 19% (22 of 116) in the CD24Fc group versus 31% (36 of 118) in the placebo group (HR 0·56, 95% CI 0·33–0·95; unadjusted p=0·031). The incidences of

adverse events and serious adverse events were similar in both groups. No treatment-related adverse events were observed. These findings suggest that targeting inflammation in response to tissue injuries might provide a therapeutic option for patients hospitalised with COVID-19.

Epidemiology

- This cohort study utilised nationwide individual-level data from the Norwegian emergency preparedness register from 1st December 2021 to 8th January 2022 and assessed the secondary attack rate of Omicron and B.1.617.2 Delta variants in households. There were 31,220 households with 1 index case, comprising 80,957 non-index members. Of the non-index household members 11,643, 41,015, and 28,299 belonged to a household in which the variant of the index case was Omicron, Delta, or non-classified, respectively. The secondary attack rate was 25.1% (95% CI, 24.4%-25.9%) when the variant of the index case was Omicron; 19.4% (95% CI, 19.0%-19.8%) when it was Delta; and 17.9% (95% CI, 17.5%-18.4%) when it was non-classified. Odds ratios were higher for men, unvaccinated individuals, and those older than 30 years, and in week 52.
- This cohort study assessed the clinical outcomes and factors associated with outcomes among children and adolescents hospitalised with COVID-19 in 6 sub-Saharan African countries (Democratic Republic of the Congo, Ghana, Kenya, Nigeria, South Africa, and Uganda). The study involved 469 children and adolescents admitted across 25 hospitals. They found relatively high morbidity and mortality, with greater likelihood of more severe outcomes among children younger than 1 year (aOR, 4.89; 95% CI, 1.44-16.61) and those with hypertension (aOR, 5.91; 95% CI, 1.89-18.50), chronic lung disease (aOR, 2.97; 95% CI, 1.65-5.37), or a haematological disorder (aOR, 3.10; 95% CI, 1.04-9.24). Eighteen patients had suspected (n = 6) or confirmed (n = 12) multisystem inflammatory syndrome in children. Age younger than 1 year (adjusted sub-distribution hazard ratio [asHR], 0.48; 95% CI, 0.27-0.87), the presence of 1 comorbidity (asHR, 0.54; 95% CI, 0.40-0.72), and the presence of 2 or more comorbidities (asHR, 0.26; 95% CI, 0.18-0.38) were associated with reduced rates of hospital discharge. Their findings suggest that COVID-19 vaccination and therapeutic interventions are needed for young populations in this region.
- This cohort study explored factors that may predict the severity of COVID-19 outcomes in 30 sickle cell patients in the United States. The patients were separated into 2 populations: those with severe COVID-19 infections (requiring hospitalisation) and those with mild/moderate COVID-19 infections. Twenty patients (67%) had mild COVID-19 disease and did not require hospitalisation. There were no patient deaths related to the diagnosis of COVID-19. Patients with HbSS had a longer average hospital stay than those with HbSC (9.14 days vs 2.67 days). Patients receiving hydroxyurea before COVID-19 infection and patients with SCD-type HbSC had significantly milder COVID-19 disease courses than those not receiving hydroxyurea or with SCD-type HbSS. A history of acute chest syndrome (ACS) appeared to be associated with a more severe COVID-19 disease course.
- This interrupted time-series study in Portugal assessed the prescription trends of anxiolytics, sedatives, hypnotics and anti-depressants in outpatient settings from January 2018 to March 2021. The authors examined whether the COVID-19 pandemic had an impact on these prescription trends or not. They found that the pandemic preceded an immediate reduction in the prescription of anxiolytics, sedatives and hypnotics for children and adolescents. However, an increasing trend throughout the pandemic was noted in the prescription of these drugs, especially among adults aged 65 years or above. A drop in anti-depressant prescription was observed as an immediate effect of the pandemic among male and female adolescents and elderly women. From March 2020 to March 2021, a decreasing prescription trend was noted among men. The impact of the pandemic on mental health and its association with the consumption trends of psychoactive drugs, and with the access to mental health treatments need further assessment.
- This review presents the key roles that mathematical modelling and quantitative analyses of empirical data have played in addressing the complex and changing dynamics of SARS-CoV-2 and ultimately to better understand and control the COVID-19 pandemic.

Infection prevention & control

- This review article demonstrates the existence of cold-chain food or packaging contamination transmission and describes the time course and epidemiological features associated with the transmission in China. Although SARS-CoV-2 on the material surface is not the main source of infection, the closed and humid environment for food packaging and transportation is a place favoring the material-to-human spread of SARS-CoV-2. In this transmission mode, patient zero is often hidden and difficult to detect, such that the outbreak usually can only be perceived after a period of a secret epidemic. Their findings suggest that regular sampling and testing of high-risk groups and imported products and proper disinfection of imported products are effective ways to detect and prevent the spread of the virus via such mode of transmission.

Non-pharmaceutical interventions, social distancing

- This study describes the initial period of the COVID-19 pandemic, along with the potential conditions and responses affecting variation in the burden of infections and severe disease burden, across the 6 island nations of the WHO's Africa region: Cabo Verde, Comoros, Madagascar, Mauritius, São Tomé e Príncipe and Seychelles. The authors analysed publicly available COVID-19 data on confirmed cases and deaths from the beginning of the pandemic through 29 November 2020. They reviewed the non-pharmaceutical response measures implemented nationally. The burden of SARS-CoV-2 infection was reduced by strict early limitations on movement and biased towards nations where detection capacity was higher. The burden of severe COVID-19 was skewed towards countries that invested less in healthcare and those that had older populations and greater prevalence of key underlying health risk factors. These findings highlight the need for Africa's island nations to invest more in healthcare and in local testing capacity to reduce the need for reliance on border closures that have dire consequences for their economies.
- This systematic review and meta-analysis of 65 studies describe the safe drinking water, sanitation and hygiene (WASH) conditions in schools in low- and middle-income countries. The studies involved 16,465 schools across 30 dfferent countries. Results indicate a lack of adequate WASH conditions in all countries. The largely insufficient and inadequate school infrastructure hampers students to practice healthy hygiene habits and handwashing in particular. In the context of the COVID-19 pandemic, being hindered to implement such a key strategy to contain the spread of SARS-CoV-2 in the school environment is of major concern.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 10th March 2022, Moderna announced the first participant has been dosed in the Phase 2 study of the Omicron-specific bivalent booster candidate (mRNA-1273.214), which combines Moderna's Omicron-specific booster candidate (mRNA-1273.529) and the Moderna COVID-19 vaccine (mRNA-1273). The study is an extension of an earlier study which aimed to evaluate the immunogenicity, safety, and reactogenicity of mRNA-1273.214 as a single booster dose in adults aged 18 years and older who previously received the two-dose primary series of mRNA-1273 and a 50 µg booster dose of mRNA-1273 with the booster dose being at least three months ago. Approximately, a total of 375 participants are expected to be enrolled at around 20 sites in the U.S. Clinical trial registration #: (NCT05249829).
- On 9th March 2022, National Institutes of Health's (NIH) launches trial to study allergic reactions to COVID-19 mRNA vaccine. Researchers from the National Institute of Allergy and Infectious Diseases (NIAID) are conducting a clinical trial designed to help understand rare but potentially serious systemic allergic reactions to COVID-19 mRNA vaccines. The single-site trial will enrol up to 100 people aged 16 to 69 years old who experienced a mild or moderate systemic allergic reaction following a first dose of either the Pfizer-BioNTech or the Moderna COVID-19 mRNA vaccine. Study participants will receive a second dose of vaccine as in-patients under carefully controlled conditions at the NIH Clinical Centre in Bethesda, Maryland. On consecutive days, each participant will be randomly assigned to receive either the FDA-approved Pfizer COVID-19 mRNA vaccine, Comirnaty, or a placebo. A phone call

follow-up interview will be done one week after discharge and thereafter an in-person follow-up in one month and five months after vaccination. At the five-month visit, all participants who tolerated the second dose of the vaccine with no or only mild symptoms will be offered a booster vaccination with the Comirnaty COVID-19 vaccine. Clinical trial registration #: (NCT04977479).

- On 8th March 2022, UC Davis Health is partnering with Pfizer on two new clinical trials to test the COVID-19 booster vaccine in healthy adults. Clinical research coordinators from the UC Davis Pulmonary and Critical Care Medicine Research Unit at Sacramento clinic are recruiting healthy adults who took two Pfizer shots, with the last one at least five months before participation. The study aims to assess the efficacy of different strength booster doses and test heart muscle protein levels after a booster shot. Participants with a history of severe allergic reaction to the vaccine or any of its components, or of COVID-19 infection are not eligible. The first study aims to test if different doses of the booster produce similar immune responses. At their first visit, participants will be randomly assigned to get either the standard 30-microgram dose or a 10-microgram dose. They will come for a total of five clinic visits over one year. The second study will analyse the levels of troponin I, a heart muscle protein, before and after a booster vaccination. High levels of troponin are linked to heart injury. Participants will get both a booster and a placebo injection, four weeks apart. They will be randomly assigned to take either of these shots at their first visit. Participation includes five visits in total over two months. Clinical trial registration #: (NCT04955626).

Therapeutics trials:

- On 11th March 2022, Fujifilm announces termination in enrolment in the currently ongoing phase 3 clinical trial in Japan for its anti-influenza drug Avigan (favipiravir), targeting patients infected with novel coronavirus infections (COVID-19). Avigan is an anti-influenza drug that had obtained domestic manufacturing and marketing approval with the treatment of new or re-emerging influenza viruses. Administration of the drug to patients is considered if a new or re-emerging influenza virus infection has occurred to which other anti-influenza virus drugs prove ineffective or produce only insufficient effects. This was a double-blind, placebo-controlled clinical trial which aimed at confirming Avigan's efficacy to prevent the progression to severe symptoms in COVID-19 patients. The primary endpoint was measured by a ratio of patients whose symptoms had become severe. Enrolment was terminated due to the fact that majority of patients recently enrolled in the trial were infected by the Omicron variant which has lower symptom severity rates than conventional variants. Clinical trial registration #: (NCT04373733).
- On 10th March 2022, Pharmazz announced U.S. Food and Drug Administration (FDA) clearance of an Investigational New Drug (IND) application for a Phase II clinical trial of centhaquine as an adjuvant to the standard of care in critically ill COVID-19 patients with acute respiratory distress syndrome ("ARDS"). Centhaquine is a resuscitative agent which acts by improving cardiac output and blood circulation without arterial constriction. It significantly improved acute respiratory distress syndrome (ARDS) and multiple organ dysfunction score (MODS) in clinical trials conducted on hypovolemic shock patients. The Phase II trial is a multicentre, randomized, double-blind, placebo-controlled study that will enrol 60 patients to assess the efficacy and safety of centhaquine to treat patients with COVID-19 and ARDS. Subjects will receive standard of care and either an intravenous dose of centhaquine, 0.01 mg/kg or a placebo. An additional dose of centhaquine will be administered if oxygenation is required or Systolic Blood Pressure (SBP) remains or falls below or equal to 90 mmHg after 24 hours of the previous dose. The primary endpoint of this trial is the improvement of PaO2/FiO2 ratio greater than or equal to 100 mmHg. Clinical trial registration #: (NCT05241067).
- On 9th March 2022, Pfizer announced that it has initiated a Phase 2/3 study to evaluate the safety, pharmacokinetics, and efficacy of PAXLOVID (nirmatrelvir [PF-07321332] tablets and ritonavir tablets) in non-hospitalised, symptomatic, paediatric participants with a confirmed diagnosis of COVID-19 who are at risk of progression to severe disease. The Phase 2/3 trial is an open-label, multi-centre, single-arm study in approximately 140 paediatric participants under 18 years of age. Initial enrolment features two cohorts; Cohort 1 includes participants aged 6 to 17 weighing at least 40 kg (88 lbs), and Cohort 2 includes those aged 6 to 17 weighing more than 20 kg (44 lbs) and less than 40 kg (88 lbs). Cohort 1 will receive PAXLOVID (nirmatrelvir/ritonavir 300 mg/100 mg) orally twice daily for five days (10 doses

total), the current authorized dosing for paediatric patients 12 years of age and older weighing at least 40kg. Cohort 2 will receive PAXLOVID (nirmatrelvir/ritonavir 150 mg/100 mg) orally twice daily for five days (10 doses total). Data from the Phase 2/3 study of non-hospitalised, high-risk adults with COVID-19 showed PAXLOVID reduced risk of hospitalisation or death by 89% (within three days of symptom onset) and 88% (within five days of symptom onset) from any cause compared to placebo, with no deaths observed in the treatment group. Treatment-emergent adverse events were comparable between PAXLOVID (23%) and placebo (24%), most of which were mild in intensity. Clinical trial registration #: (NCT05261139).

Immunotherapies trials:

- On 14th March 2022, Elektrofi & IPA announced they are entering into a collaboration to explore a high-concentration formulation of IPA's COVID-19 antibody cocktail, PolyTope (TATX-03). The aim is to generate an Investigational New Drug (IND) TATX-03E which is easily self-administered in a non-healthcare setting. The new formulation, TATX-03E, aims to address the patient need for a stable, low-volume, self-injectable formulation that is deployment ready. TATX-03E may further serve unmet patient needs by providing immune-deficient patients in need of routine administration with an at home and self-administered medication.
- On 11th March 2022, Immunome announced that the U.S. Food and Drug Administration (FDA) has lifted the clinical hold on its Investigational New Drug (IND) application for its antibody cocktail (IMM-BCP-01), for the treatment of COVID 19. This followed the FDA request for further information related to the preparation and administration of IMM-BCP-01 at clinical sites. The IND application was submitted to FDA and the plan was to initiate a placebo-controlled dose escalation study of IMM-BCP-01 in COVID 19 patients. IMM-BCP-01 is a three-antibody cocktail targeting non-overlapping regions of the spike protein of SARS-CoV-2, including highly conserved, subdominant epitopes, which elicits both ACE2 and non-ACE2 dependent neutralisation and induces natural viral clearance mechanisms, such as antibody dependent cellular cytotoxicity, complement activation and phagocytosis.
- On 3rd March 2022, Synairgen announced update on SNG001 in the ACTIV-2 Phase 3 trial for COVID-19 and on SNG001 activity against Delta and Omicron variants. SNG001 is a formulation for inhalation containing the broad-spectrum antiviral protein interferon beta. It has temporarily halted the ACTIV-2 Phase 3 clinical trial of its therapy SNG001 for COVID-19. This followed the requirement to modify the trial design due to the emergence of the SARS-CoV-2 virus' Omicron variant. The in vitro studies conducted at Viroclinics-DDL in the Netherlands have shown that SNG001 has potent antiviral activity against SARS-CoV-2 Delta and Omicron variants at concentrations that are readily achievable following inhaled delivery of interferon beta. Clinical trial registration #: (NCT04732949).
- On 2nd March 2022, Sorrento announced it has received clearance from the US Food and Drug Administration (FDA) for the commencement of a Phase 1 safety and pharmacokinetic study of its Investigational New Drug application (IND) STI-2099 (COVIDROPS) in healthy volunteers and outpatients with mild COVID-19 disease with or without a simultaneous intravenous injection of STI-2020 (COVI-AMG). STI-2099 (COVIDROPS) is a intranasal neutralising antibody against the SARS-CoV-2 virus. Initial trials are expected to be followed by a Phase 2 trial in both mild and moderate COVID-19 patients, either as a stand-alone nasal application or as a combination nasal and intravenous administration. Treatment with STI-2099 has the potential to halt the COVID-19 infection at the earliest stage in the nasal passages before it has a chance to spread to the lungs, and, if the infection has already hit the lungs, prevent the development of severe infections. Clinical trial registration #: (NCT04906694).
- On 2nd March 2022, SAB reported that National Institutes of Health's (NIH) is closing enrolment in its ACTIV-2 trial to evaluate SAB-185 treatment of COVID-19 in patients with mild and moderate infections at higher risk for progression to hospitalisation. The enrolment discontinuation are based on the fact that there are low Omicron-related COVID-19 hospitalisation and death rates that have made the current study design statistically unworkable. SAB-185 is a targeted, highly potent, fully human polyclonal antibodies that have demonstrated neutralisation of multiple SARS-CoV-2 variants in vitro, including Delta and Omicron. SAB-185 had advanced into Phase 3 after meeting pre-specified efficacy and safety criteria. Clinical trial #: (NCT04518410).

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

Contributors

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