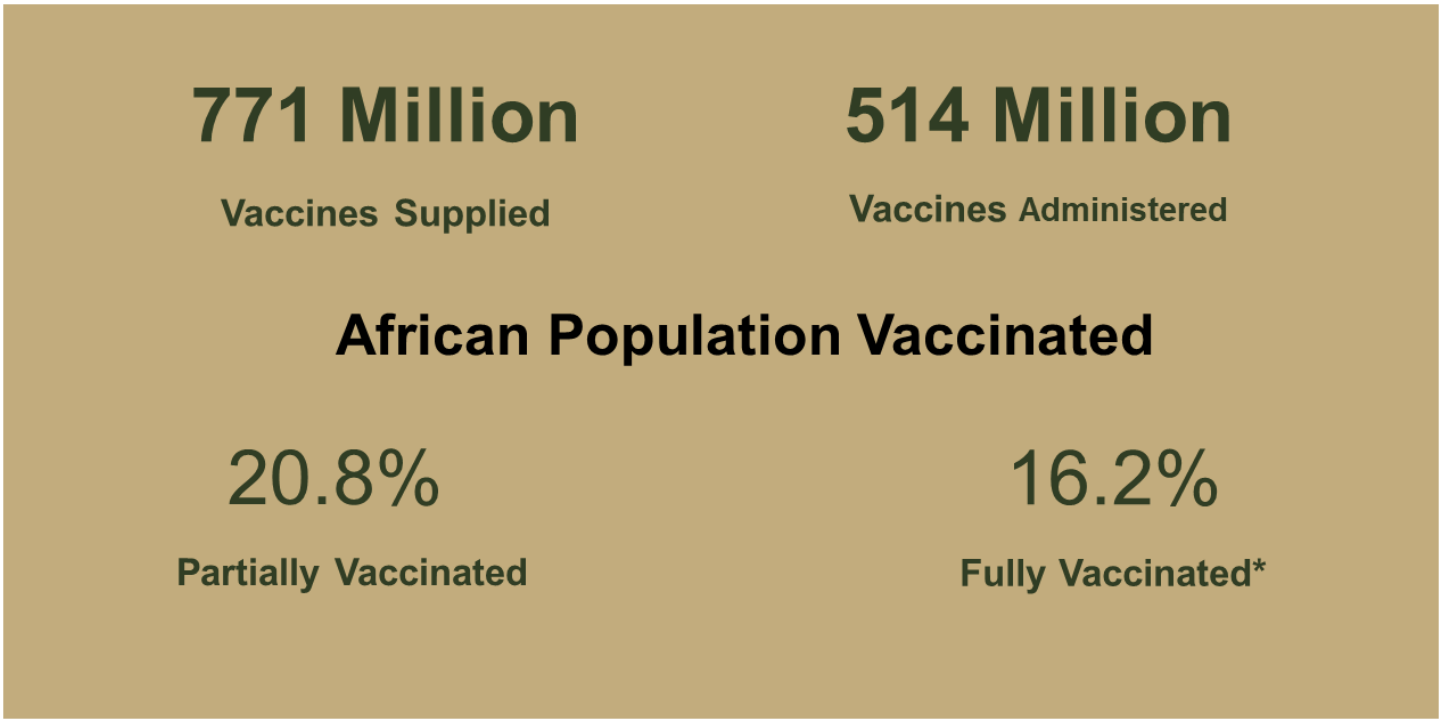
COVID-19 Scientific and Public Health Policy Update[1]

(13 April 2022)

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. This brief complements 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. Contents 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. 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

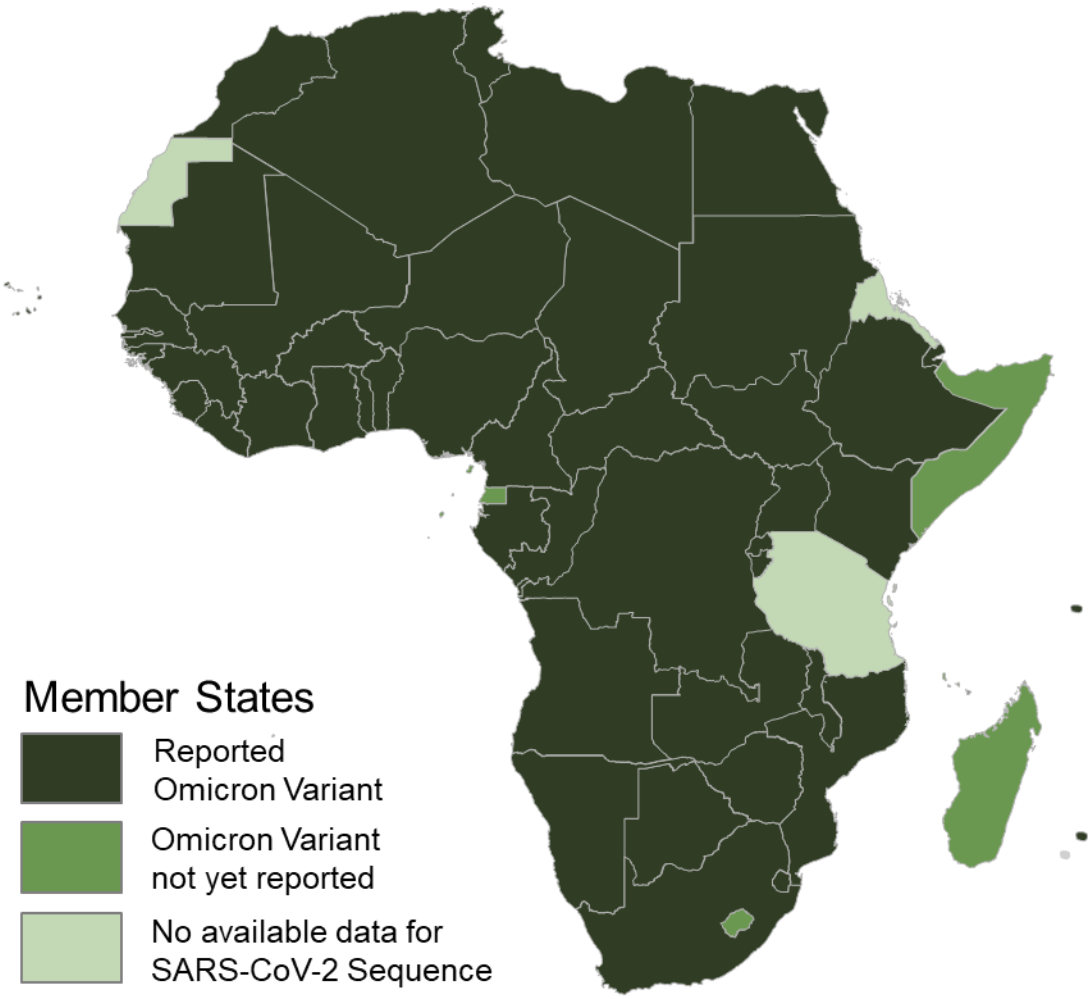


*Received two doses of a two dose COVID-19 vaccine series or one dose of the Johnson & Johnson vaccine
https://africacdc.org/COVID-19-vaccination/
Updated 13th April, 2022

[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 198 countries/territories/areas worldwide. As of 13 April 2022, 48 (87.3%) of the 55 Member States in Africa have reported this variant. For more information visit https://africacdc.org/institutes/africa-pathogen-genomics-initiative/.



Updated 13th April, 2022

B. New guidelines and resources

Since 29th March 2022,

- Africa CDC[2] has published new guidance and resources on:
  - Outbreak Brief 116: Coronavirus Disease 2019 (COVID-19) Pandemic
  - Africa CDC – Mastercard Foundation: Saving Lives and Livelihoods Newsletter

- U.S. CDC[3] has published new guidance and resources on:
  - Interim Considerations for Health Departments for SARS-CoV-2 Testing in Homeless Shelters and Encampments
  - Testing Strategies for SARS-CoV-2

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

- Collection and Submission of Postmortem Specimens from Deceased Persons with Known or Suspected COVID-19
- Evaluation for SARS-CoV-2 Testing in Animals

- WHO[4] has published new guidance and resources on:
  - Equitable access to COVID-19 tools: aligning the private sector with national response efforts
  - How to temperature map cold chain equipment and storage areas
  - Clinical care of severe acute respiratory infections – Tool kit
  - Injection safety in the context of coronavirus disease (COVID-19) vaccination: Addendum to policy brief
  - Digital documentation of COVID-19 certificates: test result: technical specifications and implementation guidance
  - Digital documentation of COVID-19 certificates: test result: web annex: DDCC:TR core data dictionary
  - Strategic preparedness, readiness and response plan to end the global COVID-19 emergency in 2022

- U.S. FDA[5] has issued press releases on:
  - On 7th April, the FDA authorised two over-the-counter (OTC) at-home COVID-19 antigen tests
  - On 7th April, the FDA authorised an extension for the shelf life of the refrigerated Janssen COVID-19 Vaccine, allowing the product to be stored at 2-8 degrees Celsius for 11 months
  - On 5th April, the FDA announced sotrovimab is no longer authorised to treat COVID-19 in any U.S. region due to increases in the proportion of COVID-19 cases caused by the Omicron BA.2 sub-variant
  - On 1st April, the FDA updated the Evusheld (tixagevimab co-packaged with cilgavimab) fact sheet with updated dosing information
  - On 31st March, the FDA revised its guidance, Emergency Use Authorisation for Vaccines to Prevent COVID-19
  - As of 12th April, 427 tests and sample collection devices are authorised by the FDA under emergency use authorisations

- ECDC[6] has issued new resources on:
  - Communicable disease threats report, 3-9 April 2022, week 14

- UKHSA[7] has issued new guidance and press releases on:
  - Guidance for people with symptoms of a respiratory infection including COVID-19, or a positive test result for COVID-19
  - COVID-19 vaccination: women of childbearing age, currently pregnant or breastfeeding
  - Reducing the spread of respiratory infections, including COVID-19, in the workplace
  - COVID-19: guidance for people whose immune system means they are at higher risk

Scientific updates

Basic Science

- This study in the United States assessed the ability of a previously identified neutralising monoclonal antibody, CV3-25, to neutralise SARS-CoV-2 variants Alpha (B.1.1.7), Delta (B.1.617.2), Gamma (P.1), and Omicron (B.1.1.529) and a more distantly related sarbecovirus from bats, WIV1. CV3-25 was previously shown to bind to the SARS-CoV-2 spike protein, neutralise the SARS-CoV-2 Beta variant

[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

comparably to the ancestral Wuhan Hu-1 strain, cross neutralise SARS-CoV-1 and bind to recombinant proteins derived from the spike-ectodomains of HCoV-OC43 and HCoV-HKU1. These findings indicate that the CV3-25 epitope is highly relevant to the development of a pan-sarbecovirus vaccine.

- This study assessed the pre-COVID-19 natural immunity among populations in central and western Africa. Sera samples (n=1655) collected before the emergence of COVID-19 from Democratic Republic of Congo, Cameroon, Republic of Congo, and Senegal were tested to detect the presence of IgG antibodies reacting against five SARS-CoV-2 proteins. Sera samples (n=189) from blood donors from France collected before the pandemic were used as controls. Antibodies against the five tested SARS-CoV-2 antigens were detected in the pre-COVID samples, with differential optical density mean value for African samples significantly higher than for the control samples. The S1 antigen showed the highest percentage of positives: 19.64% for African samples versus 2.11% for the control samples. The S2 and RBD antigens also showed significantly higher rates. Among the 1655 samples, 630 samples reacted at least against 1 antigen above the threshold (38.1%, vs. 9.5% for the controls), while 205 samples reacted at least against 2 antigens above the threshold (12.4%, vs. 0% for the controls).The results suggest that in the tested African sub-regions the populations have been potentially pre-exposed before the COVID-19 pandemic to the antigens of a SARS-CoV-2-like virus.

Vaccines

- This retrospective cohort study, based on the population of Sweden, showed that natural immunity was associated with a 95% lower risk of SARS-CoV-2 reinfection (adjusted hazard ratio [aHR]; 0.05 [95% CI 0.05–0.05]; p<0.001) and an 87% lower risk of COVID-19 hospitalisation (aHR; 0.13 [0.11–0.16]; p<0.001), compared to no immunity, for up to 20 months of follow up. In head-to-head comparisons, hybrid immunity induced by either one or two doses of a COVID-19 vaccine was associated with an additional risk reduction of SARS-CoV-2 reinfection compared with natural immunity for up to 9 months after vaccination, although with small absolute differences. Furthermore, one-dose hybrid immunity was associated with an additional 94% lower risk of COVID-19 hospitalisation HR adjusted for age and baseline date; 0.06 [95% CI 0.03–0.12]; p<0.001), and two-dose hybrid immunity with an additional 90% lower risk of COVID-19 hospitalisation (HR adjusted for age and baseline date 0.10 [0.04–0.22]; p<0.001), compared to natural immunity.
- This matched test-negative case-control study in Brazil assessed the effectiveness of four COVID-19 vaccines (CoronaVac, ChAdOx1 nCoV-19, Ad26.COV2.S, and BNT162b2) against symptomatic infection, hospitalisation, and death for individuals with previously laboratory-confirmed SARS-CoV-2 infection. The study included 22,000 RT-PCR-confirmed re-infections and more than 145,000 RT-PCR-negative controls. All four vaccines were effective against symptomatic SARS-CoV-2 infection, with effectiveness following 14 days after series completion ranging from 39.4% (95% CI 36.1–42.6) for CoronaVac to 64.8% (54.9–72.4) for BNT162b2. For vaccines with two-dose regimens, the second dose provided significantly increased effectiveness compared with one dose alone. Effectiveness against COVID-19-associated hospitalisation or death from 14 days after series completion was over 80% for CoronaVac, ChAdOx1 nCoV-19, and BNT162b2. These findings support vaccination among individuals with previous SARS-CoV-2 infection.

Diagnostics

- This diagnostic validation study in Zambia compared SARS-CoV-2 diagnostic test results from three RT-PCR assays used by the government between November 2020 to February 2021. The 3 assays (Panther Fusion® assay, Da An Gene's 2019-nCoV RNA kit and Maccura's PCR Kit) were compared with the Altona RealStar RT-PCR kit which served as the gold standard. The study included 244 participants, of which 61% (149/244) were positive by at least one PCR assay. Da An Gene, Maccura and Panther Fusion assays had sensitivities of 0.0% (95%CI 0-41%), 27.1% (95%CI 15-42%) and 76% (95%CI 65-85%) respectively but specificity was low (<85% for all three assays). The RT-PCR assays evaluated did not meet WHO recommended minimum sensitivity of 80%. Their findings highlight the need for all governments to ensure that local plans for diagnostic validation are incorporated into pandemic preparedness planning.
- This study in Australia presented an automated, high-throughput integrated screening platform, incorporating saliva-based loop-mediated isothermal amplification (LAMP) technology, that was

designed for population-scale sensitive detection of infectious carriers of SARS-CoV-2 RNA. Central to this surveillance system is the "Sentinel" testing instrument, which is capable of reporting results within 25 min of saliva sample collection with a throughput of up to 3840 results per hour. The instrument incorporates continuous flow loading of samples at random intervals to cost-effectively adjust for fluctuations in testing demand. Independent validation of the saliva-based RT-LAMP technology on an automated LAMP instrument suggested 98.7% sensitivity, 97.6% specificity, and 98% accuracy against a RT-PCR comparator assay. The platform offers a feasible and scalable approach to complement vaccination, to curb the spread of COVID-19 variants, and control future pandemics.

Care and Treatment

- This systematic review and bayesian meta-analysis of 3 randomised clinical trials assessed the evidence for fluvoxamine in the outpatient management of COVID-19. The trials included 2,196 adults with COVID-19 who each received a twicedaily dose of fluvoxamine 50 mg. Under a variety of assumptions, the probability that fluvoxamine was associated with reduced hospitalisation ranged from 94.1% to 98.6% and the probability of moderate association ranged from 81.6% to 91.8%. Ongoing randomised trials are important to evaluate alternative dosing strategies, explore the effectiveness in vaccinated patients, and provide further refinement to these estimates. Meanwhile, fluvoxamine could be recommended as a management option, particularly in resource-limited settings or for individuals without access to SARS-CoV-2 monoclonal antibody therapy or direct antivirals.
- This multicenter, double-blind, randomised, controlled trial in the United States assessed the efficacy and safety of COVID-19 convalescent plasma in symptomatic adults who had tested positive for SARS-CoV-2. The study included 1,181 participants from 23 sites. Of these participants, 592 received convalescent plasma and 589 received control plasma. Hospitalisation occurred in 17 of 592 participants (2.9%) who received convalescent plasma and 37 of 589 participants (6.3%) who received control plasma (absolute risk reduction, 3.4%; 95% CI, 1.0 to 5.8; p=0.005), which corresponded to a relative risk reduction of 54%. Evidence of efficacy in vaccinated participants cannot be inferred from their results. Sixteen (16) grade 3 or 4 adverse events (7 in the convalescent-plasma group and 9 in the control-plasma group) occurred in participants who were not hospitalised.
- This multicenter matched case-control study in Italy assessed the effect of the sofosbuvir/velpatasvir (SOF/VEL) combination provided early during an SARS-CoV-2 infection. The study included 120 patients with mild or moderate COVID-19, of whom 30 received SOF/VEL tablets (400/100 mg) once daily for 9 days within a median of 6 days from the beginning of infection, and 90 controls (matched for age, sex, duration of infection and comparable clinical condition) who were treated with standard of care. Between 5–14 days after starting SOF/VEL, SARS-CoV-2 clearance was observed in 83% of patients in the treatment group, while spontaneous clearance in the control was 13% ($p < 0.001$). Earlier SARS-CoV-2 clearance was observed in the SOF/VEL group than in the control group (median 14 vs 22 days, respectively, $p < 0.001$) also when the first positivity was considered. None of the patients in the SOF/VEL group showed disease progression, while in the control group, 24% required more intensive treatment (high flow oxygen or noninvasive/invasive ventilation), and one patient died ($p < 0.01$). No significant side effects were observed in the SOF/VEL group.The results indicate that early SOF/VEL treatment in mild/moderate COVID-19 seems to be safe and effective for faster elimination of SARS-CoV-2 and to prevent disease progression.

Epidemiology

- This study assessed the relationship between SARS-CoV-2 load in urban wastewater and surveillance indicators of infection prevalence and severity in Milan, Italy. Sewage samples were collected approximately once a week from March 2020 to November 2021 in the Nosedo wastewater treatment plant, serving about 50% of the Milan population. The SARS-CoV-2 load in wastewater was compared spatially with surveillance indicators of infection prevalence (number of positive cases and hospitalised patients per day). The curves for wastewater load and hospitalised patients were similar until the increase in vaccination coverage. The curves for wastewater load and positive cases were also similar except during the first wave, which was characterized by a shortage of tests. Curves for positive cases

and hospitalisations diverged from the curve for wastewater load as vaccination coverage increased, with decreases in cases and hospitalisations and increases in wastewater viral load. These results suggest that vaccines are effective in protecting against symptomatic and severe disease, but that, with high vaccination rates, standard surveillance metrics may not accurately estimate the spread of SARS-CoV-2. Thus, wastewater surveillance may be important as an early warning of virus circulation.

- This cohort study in the United States of America assessed the incidence rates and clinical outcomes of Omicron infection before and after Omicron became the predominant variant in the US (1 September, 2021, and 31 January, 2022). The study included 651,640 children < 5 years of age with no prior SARS-CoV-2 infection. The monthly incidence rate of SARS-CoV-2 infections was mostly stable (1.0-1.5 cases per 1000 persons per day) between September and November 2021 (Delta-predominant period) but rapidly increased to 2.4 to 5.6 cases per 1,000 persons per day in December 2021, coinciding with the emergence of Omicron variant. Monthly incidence rates of SARS-CoV-2 infections peaked at 8.6 cases per 1,000 persons per day in the first half of January 2022 (Omicron-predominant period) and 8.2 in the second half of January 2022. During this same time period, risks for severe clinical outcomes in children infected with Omicron variant were significantly lower than those in the matched Delta cohort. (Hazard Ratio [95% CI]; emergency department visits; 0.84 [0.80-0.87], hospitalisations; 0.66 [0.58-0.74], intensive care unit admissions; 0.35 [0.25-0.51], and mechanical ventilation; 0.15 [0.07-0.33]).
- This cross-sectional study in Colombia describes the molecular epidemiology of the SARS-CoV-2 Mu variant in Antinoquia State. Nasopharyngeal swabs or bronchoalveolar wash samples were obtained from patients with suspected SARS-CoV-2 infection who presented to health facilities from July 2020 through August 2021. A total of 1,032 viral samples were obtained for whole-genome sequencing. The Mu variant was first detected in Antioquia in March 2021. By July 2021, this variant accounted for 52 (85.2%) SARS-CoV-2 genome sequences, coinciding with the largest wave of COVID-19 cases reported in the country since the start of the pandemic. The prevalence of the Mu variant decreased to 34 (55.7%) sequences in August 2021, coinciding with the introduction of the Delta variant. Except for clinical outcomes, no differences in age, sex, or risk factors were detected among persons infected with the Mu variant compared to those infected other variants circulating at the time
- This study identified 21 predetermined country-level factors that explained marked variations in weekly COVID-19 morbidity and mortality across 91 countries between January and the end of 2020. Besides factors commonly associated with infectious diseases (e.g., population and tourism activities), results from the analysis listed country characteristics that influenced COVID-19 disease outcomes. Characteristics were grouped into demographic-geographic, political-legal, socio-economic and healthcare factors. Findings have implications for policymakers, healthcare experts, and public. policymakers. These factors could be incorporated into strengthening community-based approaches in risk-preparedness and social solidarity during future health crises.

Infection prevention & control

- This multicenter cross-sectional study assessed the knowledge, attitude, and practice (KAP) and factors associated with infection prevention and control practices towards COVID-19 among healthcare providers (HCP) in Amhara region, Ethiopia. The study included 422 HCPs in public health facilities, between 20th September and 20th October 2020. Overall, 368 (89.8%), 387 (94.4%), and 326 (79.5%) of the surveyed HCPs had adequate knowledge, positive attitude, and good prevention practices towards COVID-19, respectively. Factors significantly associated with good COVID-19 prevention practice were being a Nurse (AOR = 2.13, 95% CI = 1.13–3.99), having < 5 years of work experience (AOR = 0.46, 95% CI = 0.24–0.86), using social media (AOR = 6.20, 95% CI = 2.33–16.51) and relying on television and/or radio (AOR = 4.03, 95% CI = 1.56–10.38) as sources of COVID-19 information.
- This study in South Korea described the development of a novel skin sanitizing solution that exhibited antimicrobial effects against COVID-19 for a sufficient period of time. Plasma-activated water (PAW) was produced by dissolving reactive nitrogen oxide gas using microwave plasma in deionized water. The solution had a 99.99% sterilization effect after conducting viral titers with Vero-E6 cells infected with SARS-CoV-2 and treated with a mixture of SARS-CoV-2 and 5 × PAW. The solution also reduced *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Bacillus cereus,* and *Salmonella*

typhimurium by 99.99%. PAW was also non toxic to normal skin cells. These findings support the use of PAW as an effective skin disinfectant in the current situation of a global pandemic.

- This cross-sectional study assessed the extent and dynamics of the COVID-19 pandemic within the prison system of Lombardy, Italy and reports the infection prevention and control measures implemented. The study was carried out from 1 March, 2020, through 28 February, 2021 (first wave, March-June 2020; second wave, October 2020-February 2021). The study included 7,599 incarcerated individuals and 4,591 prison staff across 18 detention facilities. During the study, 1,564 incarcerated individuals and 661 prison staff were diagnosed with COVID-19. Most cases were reported during the second wave (1,474 in incarcerated individuals, 5,29 in prison staff), following relaxation of the previously enforced mitigation measures. Incarcerated individuals and prison staff had a higher relative risk for COVID-19 infection than the general population during both the first wave (incarcerated individuals: 1.30; 95% CI, 1.06-1.58; prison staff: 3.23; 95% CI, 2.74-3.84) and the second wave (incarcerated individuals: 3.91; 95% CI, 3.73-4.09; prison staff: 2.61; 95% CI, 2.41-2.82). Findings suggest that prison settings should be included and prioritised in the framework of emergency preparedness and response.

Non-pharmaceutical interventions, social distancing

- This simulation modelling study projected COVID-19 deaths between 1 March and 31 December, 2022, in each of the 50 US states, District of Columbia, and Puerto Rico assuming different dates of lifting of mask mandates and nonpharmacologic interventions (NPIs). With the high transmissibility of current circulating SARS-CoV-2 variants, the simulated lifting of NPIs in March 2022 was associated with resurgences of COVID-19 deaths in nearly every state. In comparison, delaying by even 1 month to lift NPIs in April 2022 was estimated to mitigate the amplitude of the surge. For most states, however, no amount of delay was estimated to be sufficient to prevent a surge in deaths completely. The primary factor associated with recurrent epidemics in the simulation was the assumed high effective reproduction number of unmitigated viral transmission. With a lower level of transmissibility similar to those of the ancestral strains, the model estimated that most states could remove NPIs in March 2022 and likely not see recurrent surges.
- This systematic review and meta-analysis of 26 studies assessed the physiological responses to the use of face masks. The studies included a total of 751 participants. The use of face masks was not associated with significant changes in pulsoxymetrically measured oxygen saturation, even during maximal-effort exercises. The only significant physiological responses to the use of face masks during low-intensity activities a slight increase in heart rate (standardized mean difference (SMD) 0.30, confidence interval (CI) 0.08; 0.51), mildly elevated partial pressure of carbon dioxide (SMD 0.53, CI 0.09; 0.97), increased temperature of facial skin covered by the mask (SMD 1.05, CI 0.48; 1.63), and subsequent increase of the score in the rating of heat perception (SMD 1.04, CI − 0.12; 2.19), with N95 filtering facepiece respirators having a greater effect than surgical masks. In high-intensity conditions, the use of face masks was associated with decreased oxygen uptake (SMD − 0.44; CI − 0.77, − 0.11), ventilation (SMD − 0.65; CI − 0.73, − 0.57), and respiratory rate (SMD − 0.07; CI − 0.31, 0.17).

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 7th April 2022, Akston announced the first volunteers in a Phase 2/3 clinical trial of AKS-452. AKS-452 is a protein subunit, thermostable and shelf stable designed to induce a Th1/Th2 mixed immune response in COVID 19 patients against the Receptor Binding Domain (RBD) of the novel coronavirus spike protein. The treatment does not include mRNA technology, viral vectors, or a weakened SARS-CoV-2 virus and has been engineered to use established, low-cost antibody manufacturing techniques. A total of 1,500 healthy volunteers are expected to participate in a Phase 2/3 double-blind placebo-controlled study in India. The primary objective of the study is to evaluate the safety, tolerability and humoral immunogenicity profile (i.e., SP/RBD-specific IgG titers) of AKS-452 at day 56, following a two-injection regimen in a combined bridging and a Phase 2/3 clinical study. Clinical trial registration #: (NCT05124483).

- On 6th April 2022, The University of California San Diego has joined a Phase 2 clinical trial to evaluate various additional COVID-19 booster shots. The COVID-19 Variant Immunologic Landscape trial (COVAIL) seeks to understand if different vaccine regimens can broaden immune responses in adults who already have received a primary vaccination series and a first booster shot. Despite waning protection against infection and mild illness during the Omicron wave, COVID-19 vaccines available in the United States have thus far maintained durable protection against severe COVID-19. The concern is that future variants may evade protection provided by currently available COVID-19 vaccines. The COVAIL study will evaluate the safety and immunogenicity of additional doses of prototype and variant vaccine candidates in previously vaccinated participants with or without prior SARS-CoV-2 infection. The study will evaluate innate, cellular and humoral immune responses to inform on how to shift the immune response to cover new variants as they emerge.
- On 5th April 2022, Tonix announced a new preclinical research agreement with Kansas State University (K-State) to extend the research to develop a vaccine candidate for the prevention of COVID-19 that utilizes a novel live virus vaccine vector platform, bovine parainfluenza virus. The research will also test the effect of co-expression of the CD40-ligand, also known as CD154 or 5c8 antigen, to stimulate T cell immunity. TNX-2300 is an investigational new biologic at the pre-IND stage of development and has not been approved for any indication. TNX-2300 is a live replicating virus vaccine designed potentially to elicit T cell immunity against the SARS-CoV-2 spike protein. The technology also includes a molecular stimulant called CD40-ligand, which triggers strong immunity, including T cell responses. Attenuated bovine parainfluenza virus has previously been shown to be an effective antigen delivery vector in humans. Vaccines based on live replicating viruses trigger the immune system by direct stimulation of T cells, with the potential to elicit strong, long-lasting and durable immunity.
- On 4th April 2022, The World Health Organization (WHO) has issued an updated Emergency Use Listing (EUL) for the Johnson & Johnson COVID-19 vaccine, recommending the vaccine for use in boosted regimens in persons aged 18 years and older. The updated EUL recommends the Johnson & Johnson COVID-19 vaccine be used both as a homologous booster (same vaccine) after a single-dose primary vaccination and as a heterologous booster ('mix-and-match' vaccines) following a primary mRNA vaccine regimen. The WHO has also recommended to extend the shelf-life of thawed vaccine stored at 2 to 8 degrees Celsius (36 to 46 degrees Fahrenheit) to 11 months, remaining within the vaccine's maximum 24-month shelf-life when stored at -25 to -15 degrees Celsius.
- On 31st March 2022, Novavax announced submission of the request to expand the conditional marketing authorisation (CMA) of Nuvaxovid (NVX-CoV2373) COVID-19 Vaccine (recombinant, adjuvanted) in the European Union (EU) to adolescents aged 12 through 17 years. The submission includes clinical data from the ongoing pediatric expansion of PREVENT-19, a pivotal Phase 3 trial of 2,247 adolescents aged 12 through 17 years across 73 sites in the U.S.. The expansion will be used to evaluate the safety, effectiveness (immunogenicity), and efficacy of Novavax' COVID-19 vaccine. The vaccine achieved its primary effectiveness endpoint in the trial and demonstrated 80% efficacy overall at a time when the Delta variant was the predominant circulating strain in the U.S. Additionally, preliminary safety data from the pediatric expansion of PREVENT-19 showed the vaccine to be generally well-tolerated. Serious and severe adverse events were low in number and balanced between vaccine and placebo groups, and not considered related to the vaccine. Clinical trial registration #: (NCT04611802).
- On 29th March 2022, Pfizer and BioNTech announced the U.S. Food and Drug Administration (FDA) has expanded the emergency use of Pfizer-BioNTech COVID-19 vaccine to include a second booster dose in adults ages 50 years and older who have previously received a first booster of any authorised COVID-19 vaccine. The FDA also has authorised a second booster dose for individuals 12 years of age and older who have certain kinds of immunoncomprised conditions and have previously received a first booster dose of any authorised COVID-19 vaccine. The additional booster will be administered at least four months after the first booster using the same formulation and strength as prior Pfizer-BioNTech COVID-19 vaccine doses. The expanded EUA is based on the totality of scientific evidence shared including immunogenicity data from an ongoing, open-label study in 154 healthcare workers ≥18 years of age at a single center in Israel who received two booster doses during a period when Omicron was the predominant variant. Approximately 11-fold increases in geometric mean neutralising

antibody titers against wild-type virus, Delta and Omicron variants, respectively, were reported at two weeks after the second booster as compared to 5 months after the first booster dose. No new safety concerns were noted among study participants. Data also shows a decline in vaccine effectiveness against COVID-19 three to six months after the initial booster. Evidence from Israel suggests that an additional booster dose can improve protection against severe disease and death.

Therapeutics trials:

- On 11th April 2022, Veru announced positive efficacy and safety results of the oral sabizabulin from a planned interim analysis of 150 hospitalised COVID-19 patients at high risk for Acute Respiratory Distress Syndrome (ARDS). The Phase 3 COVID-19 study is a double-blind, randomised, placebo-controlled clinical trial evaluating oral, once-a-day dosing of sabizabulin 9 mg versus placebo in approximately 210 hospitalised moderate to severe COVID-19 patients (≥WHO 4) who were at high risk for acute respiratory distress syndrome (ARDS) and death. Patients were randomised in a 2:1 ratio to the sabizabulin treatment group versus placebo. Patients in both treatment groups were allowed to receive standard of care including remdesivir, dexamethasone, anti-IL6 receptor antibodies, and JAK inhibitors. The trial was conducted in the United States, Brazil, Colombia, Argentina, Mexico, and Bulgaria. COVID-19 infections treated in the study included the Delta and Omicron variants. The prespecified primary endpoint was death at or before day 60. Sabizabulin treatment resulted in a clinically and statistically meaningful 55% relative reduction in deaths (p=0.0029) in the intent to treat population. Placebo group (n=52) had a 45% mortality rate compared to the sabizabulin-treated group (n=98) which had a 20% mortality rate. Clinical trial registration #: (NCT04842747).
- On 6th April 2022, Tonix announced the U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application to support a Phase 2 clinical trial with TNX-102 SL as a potential treatment for a subset of patients with Long COVID Syndrome (Long COVID) whose symptoms overlap with fibromyalgia. Post-Acute Sequelae of COVID-19 (PASC) can persist for many months and can range from mild to incapacitating. PASC can include fatigue, multi-site pain, sleep disturbances, fevers, shortness of breath, cognitive impairment, gastrointestinal symptoms, anxiety and depression. The Phase 2 study will be a double-blind randomised, placebo-controlled 14-week trial to evaluate the safety and efficacy of sublingual TNX-102 SL 5.6 mg daily at bedtime in the treatment of patients with multi-site pain associated with Long COVID. Approximately 470 patients (235 per arm) will be enrolled from across 30 trial sites and randomised in a 1:1 ratio to treatment with TNX-102 SL or placebo tablets. The primary efficacy endpoint will be Change from Baseline in the weekly average of daily self-reported worst pain intensity scores at the Week 14 endpoint.
- On 6th April 2022, Kintor announced top-line results of the Phase 3 MRCT of proxalutamide in outpatients with mild to moderate COVID-19 regardless of vaccination status and risk factors. Proxalutamide is an ACE2 (angiotensin-converting enzyme 2) and TMPRSS2 (transmembrane protease, serine 2) proteins inhibitor that inhibits the entry of the SARS-CoV-2 virus into host cells. The treatment also promotes the clearance of pathogens and decreases inflammation by activating the Nrf2 pathway, which inhibits the over-production of IL-6, proinflammatory cytokines, and chemokines, thus minimizing cytokine storms and tissues damage. The phase 3 multi-center randomised, double-blind, placebo-controlled (1:1) trial evaluated the efficacy and safety of proxalutamide in 733 outpatients with mild to moderate COVID-19 illness. Data from the study demonstrated that the protection rate of patients in the trial (regardless of age or risk factors) treated with proxalutamide for more than seven days reached 100% ($p < 0.02$). Treatment with proxalutamide significantly reduced hospitalisation and death in COVID-19 patients, especially among cases who were middle-aged and elderly with high-risk factors. Ninety-nine percent (99%) of the patients were recruited in the United States. The patients received either proxalutamide 200mg, once daily plus standard of care (SOC) “proxalutamide arm”or placebo plus SOC “placebo arm”for 14 consecutive days. The study demonstrated that proxalutamide was well tolerated and side effects were manageable in patients with mild to moderate COVID-19. Clinical trial registration #: (NCT04870606).
- On 4th April 2022, Aligos announced that it has selected ALG-097558, a broad spectrum coronavirus protease inhibitor, as the drug candidate to move forward into development. The program is part of the collaboration and license agreement with KU Leuven, including the Centre for Drug Design and

Discovery (CD3), a drug discovery unit and investment fund of KU Leuven, and the Rega Institute for Medical Research. ALG-097558 has shown superior potency compared to nirmatrelvir (PF-07321332) against SARS-CoV-2 and multiple resistant variants in all cell-based assays tested to date. ALG-097558 is 9 to 20-fold more active than nirmatrelvir, depending on the variant. Evaluation against the Omicron variant demonstrates a 10-fold improvement in cell-based potency for ALG-097558 compared to nirmatrelvir. ALG-097558 exerts potent broad spectrum activity against alpha and beta coronaviruses, and its highly conserved target site indicates a high probability that it will retain potent activity against potential future SARS-CoV-2 variants. Projected efficacious doses of ALG-097558 can be achieved in humans without ritonavir boosting. A Phase 1 clinical trial application is expected to be filed this year (2022).

Immunotherapies trials:

- On 5th April 2022, US Food and Drug Administration (FDA) has updated the emergency use authorisation (EUA) for GlaxoSmithKline (GSK) and Vir Biotechnology's sotrovimab and suspended the use of sotrbovimap to treat Covid-19. Sotrovimab is an investigational monoclonal antibody that binds to the epitope of the SARS-CoV-2 virus to neutralise it. The suspension follows an analysis from the Centers for Disease Control and Prevention (CDC) indicating that more than 50% of COVID-19 cases in the U.S. are current caused by of the Omicron BA.2 sub-variant. The regulatory authority noted that the antibody is unlikely to be effective against the Omicron BA.2 sub-variant, which is causing a rise in the number of Covid-19 cases across all Health and Human Resources Regions.
- On 4th April 2022, Roche announced that the U.S. Food and Drug Administration (FDA) has accepted the supplemental Biologics License Application (sBLA) and has granted Priority Review for Actemra/RoActemra (tocilizumab) intravenous for the treatment of COVID-19 in hospitalised adults who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation. The sBLA submission is based on results from four randomised, controlled studies that evaluated Actemra/RoActemra for the treatment of COVID-19 in more than 5,500 hospitalised patients. Altogether, the results of these four studies (EMPACTA, COVACTA, REMDACTA, and RECOVERY) suggest that Actemra/RoActemra may improve outcomes in patients receiving corticosteroids and requiring supplemental oxygen or breathing support. Clinical trial registration #: (NCT04372186, NCT04320615, NCT04409262 and NCT04822818).
- On 31st March 2022, ARCA has reported topline results from Phase 2b ASPEN-COVID-19 clinical trial of its therapy rNAPc2 (AB201) to potentially treat hospitalised Covid-19 patients. rNAPc2 (AB201) is a highly selective tissue factor inhibitor which has anti-inflammatory, anticoagulant and potential antiviral effects. This is a multicentre, randomised trial assessed two doses of rNAPc2 versus standard of care of heparin in 160 Covid-19 hospitalised patients with increased D-dimer levels. D-dimer is a biomarker that is utilised to evaluate coagulation activation and usually is raised in hospitalised Covid-19 patients and linked to adverse clinical outcomes. The pooled lower and higher rNAPc2 dose arms showed a decline compared to baseline in D-dimer levels of 16.8% versus 11.2% in the heparin arm which was not statistical significance for the primary efficacy endpoint. The therapy (rNAPc2) was well tolerated at both doses. Clinical trial registration #: (NCT04655586).
- On 31st March 2022, Sorrento announced that the FDA has given clearance to launch the Phase 3 clinical trial of Abivertinib in severe COVID-19 patients (hospitalised patients with respiratory compromise requiring oxygen supplementation). Abivertinib is a novel dual target, small molecule tyrosine kinase inhibitor (TKI) designed to selectively target mutant forms of the epidermal growth factor receptor (EGFR) and Bruton's tyrosine kinase (BTK). The clearance based on preliminary results from two Phase 2 studies demonstrating that hospitalised COVID-19 patients with severe pneumonia, especially those requiring non-invasive ventilation or high flow oxygen supplementation, were up to 5-fold more likely to benefit from Abivertinib therapy than those patients who required low flow supplementation. The phase 3 study will be conducted at multiple sites in the USA, Mexico and Brazil.
- On 30th March 2022, Adagio reported the primary endpoints were met with statistical significance for all three indications in the ongoing global Phase 2/3 clinical trials evaluating its investigational drug adintrevimab (ADG20) as a pre-and-post-exposure prophylaxis (EVADE) and treatment (STAMP) for

COVID-19. Adintrevimab is an investigational monoclonal antibody designed to be a potent, broadly neutralising antibody for both the prevention and treatment of COVID-19, including disease caused by most variants, as either a single or combination agent. Results showed risk of symptomatic COVID-19 was reduced by 71% compared to placebo in pre-exposure prophylaxis and 75% compared to placebo in post-exposure prophylaxis. Risk of hospitalisation or death in participants with mild to moderate COVID-19 was reduced by 66% compared to placebo in the primary efficacy analysis population and by 77% compared to placebo in participants who received treatment within three days of symptom onset. Clinical trial registration #: (NCT04859517).

- On 28th March 2022, AptaTargets announces it has dosed the first patient in the clinical trial with the drug ApTOLL for treating COVID-19 at the University Hospital La Princesa in Madrid (Spain). This patient is in Phase 1b of aptaCovid, a randomised, blind, multicentre, placebo-controlled clinical trial that includes 30 patients hospitalised with COVID-19 and are at-risk of developing cytokine storm syndrome (an excessive and uncontrolled inflammatory process following infection). The aim of aptaCovid is to evaluate the safety and efficacy of ApTOLL. ApTOLL is a novel single-stranded DNA molecule (aptamer) with immunomodulator and anti-inflammatory effect. The drug's activity focuses on blocking the activation of TLR4, a receptor located on the surface of immune cells responsible for initiating the inflammatory cascade. Upon blocking this activation, ApTOLL modulates the inflammatory response, and therefore, prevents the development of the cytokine storm syndrome in the most severe COVID-19 cases. ApTOLL has shown efficacy in preclinical studies for ischaemic stroke, haemorrhagic stroke, myocardial infarction and multiple sclerosis, and has an excellent safety profile in Phase I and Phase Ib clinical trials on healthy volunteers and patients with ischaemic stroke. Clinical trial registration #: (NCT05293236).

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

Contributors

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