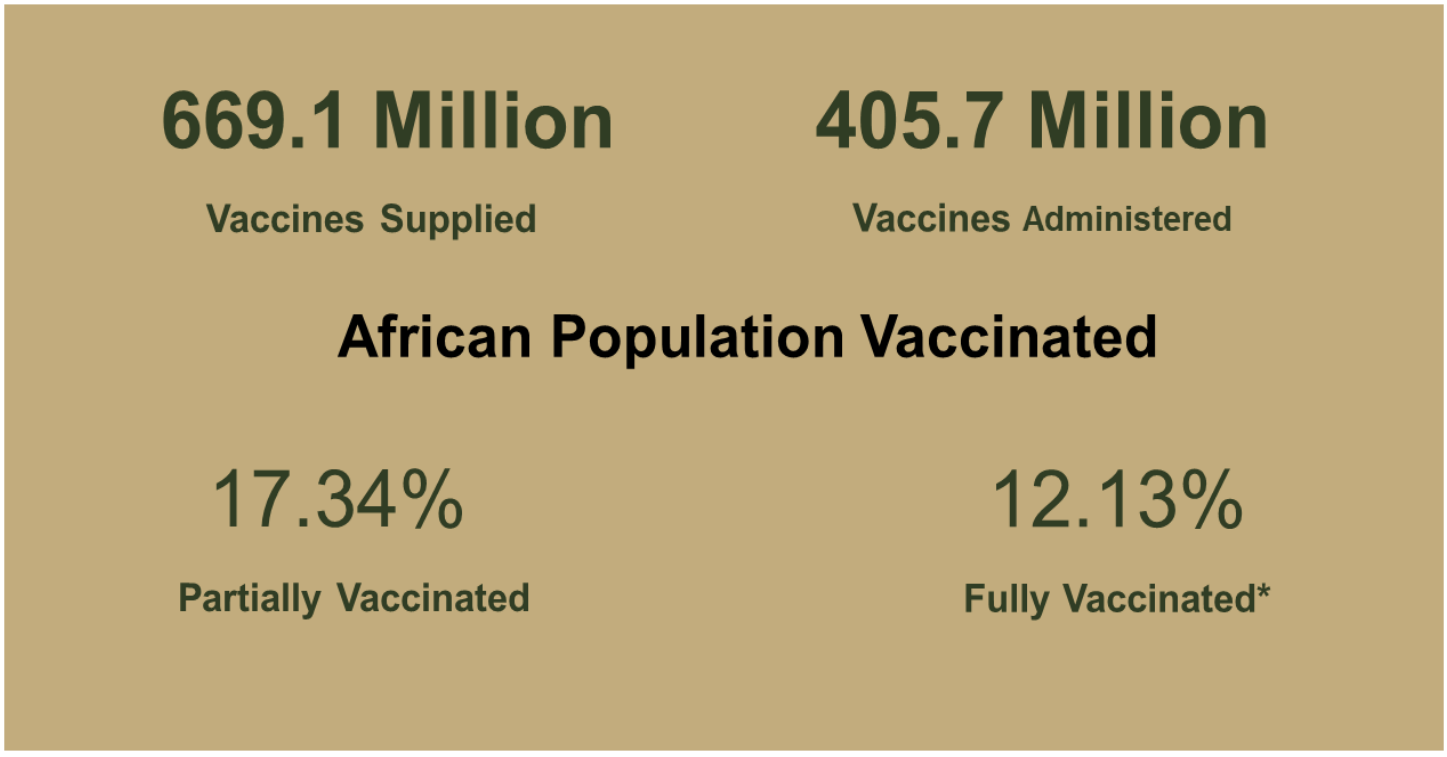
COVID-19 Scientific and Public Health Policy Update[1]

(16 February 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 in these areas.*

A. Trending Topics

Status of Vaccines in Africa

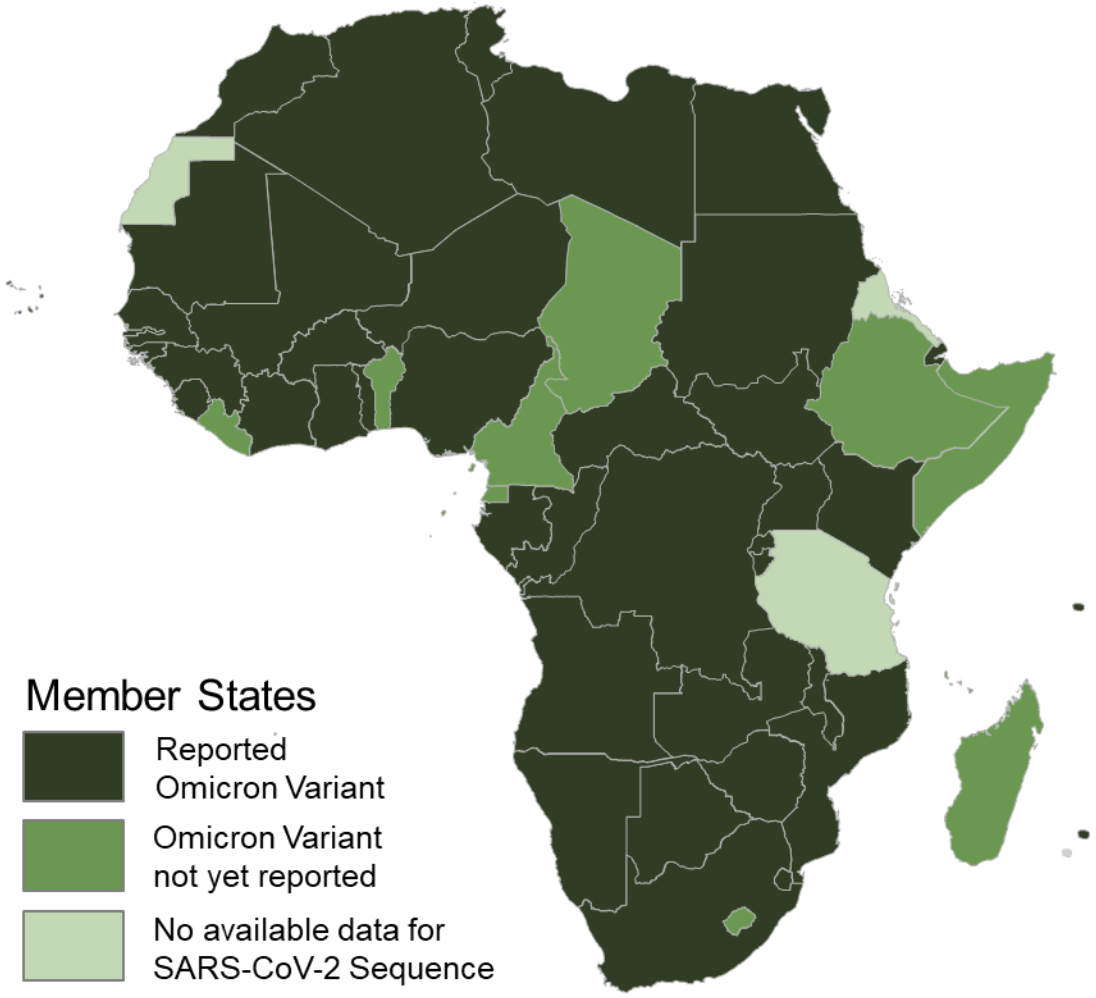


*Received two doses of a two dose COVID-19 vaccine series or one dose of the Johnson & Johnson vaccine
https://africacdc.org/COVID-19-vaccination/
Updated 16th February, 2022

[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

- The Omicron variant (B.1.1.529), first reported in South Africa on 24th November 2021, has spread to 175 countries worldwide; 41 (75%) of the 55 Member States in Africa have reported this variant. https://africacdc.org/institutes/africa-pathogen-genomics-initiative/



Updated 16th February, 2022

B. New guidelines and resources

Since 1st February 2022,

- Africa CDC[2] has published new guidance and resources on:
  - Guidance on administration of COVID-19 vaccine boosters in Africa
  - Outbreak Brief 109: Coronavirus Disease 2019 (COVID-19) Pandemic

- U.S. CDC[3] has published new guidance and resources on:
  - Interim Guidance on Management of Coronavirus Disease 2019 (COVID-19) in Correctional and Detention Facilities

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

- Scaling Up Staffing Roles in Case Investigation and Contact Tracing
- Contact Tracing for COVID-19
- Operational Considerations for Immunization Services during COVID-19 in Non-US Settings Focusing on Low-Middle Income Countries
- How to Determine a Close Contact for COVID-19
- Considerations for Institutes of Higher Education

- WHO[4] has published new guidance and resources on:
  - Contact tracing and quarantine in the context of the Omicron SARS-CoV-2 variant: interim guidance
  - Questions and Answers: COVID-19 vaccines and pregnancy
  - Public health surveillance for COVID-19: interim guidance
  - Operational guidance on establishing an ultra-cold chain system in support of the Pfizer-BioNTech COVID-19 vaccine rollout
  - COVID-19 clinical care pathway (CARE): confirm, assess, respond, evaluate
  - COVID-19 clinical care pathway (CARE): confirm SARS-CoV-2 infection, assess symptoms, risk factors and severity, respond with appropriate care and treatment, evaluate clinical response and recovery

- U.S. FDA[5] has issued press releases on:
  - On 8th February, FDA issued a guidance for industry and investigators titled COVID-19 Public Health Emergency: Policy on COVID-19-Related Sanitation Tunnels
  - On 11th February, FDA authorises new monoclonal antibody for treatment of COVID-19 that retains activity against Omicron variant
  - On 11th February, FDA postpones Advisory Committee Meeting to discuss request for authorisation of Pfizer-BioNTech COVID-19 Vaccine for children 6 months through 4 years of age
  - As of 15th February, 421 tests and sample collection devices are authorised by the FDA under emergency use authorisations

- ECDC[6] has issued new resources on:
  - Considerations for the use of antibody tests for SARS-CoV-2 – first update
  - COVID-19 vaccine effectiveness in adolescents aged 12–17 years and interim public health considerations for administration of a booster dose
  - Considerations for the use of face masks in the community in the context of the SARS-CoV-2 Omicron variant of concern
  - Evaluation of the SARS-CoV-2 testing policy in Belgium from June to December 2021

- UKHSA[7] has issued new guidance and press releases on:
  - COVID-19 test validation approved products
  - National protocol for COVID-19 Vaccine AstraZeneca (ChAdOx1-S [recombinant])
  - COVID-19 vaccination: blood clotting information for healthcare professionals
  - Coronavirus (COVID-19) testing for staff after international travel
  - COVID-19 vaccination: information for healthcare practitioners

[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

Scientific updates

Basic Science

- The authors of this study utilised plasma obtained from 20 unvaccinated and 7 vaccinated individuals infected in the fourth wave of the COVID-19 pandemic in South Africa to assess the cross-reactivity against different Variants of Concern (VOCs) for binding, Fc effector function and neutralisation. Individuals were recruited at a time when Omicron was responsible for >90% of infections. Among unvaccinated individuals, the Fc effector function and binding antibodies targeted Omicron and other VOCs at comparable levels. However, Omicron-triggered neutralisation was not extensively cross-reactive to VOCs, with 20 to 43-fold reductions in titre. Among vaccinated individuals, breakthrough Omicron infection improved cross-neutralisation of VOCs, with titres exceeding 1:2,900. Their findings imply that unvaccinated Omicron-infected individuals are vulnerable to reinfection by circulating and emerging VOCs. Further, while Omicron-based immunogens may act as adequate boosters, they are unlikely to be superior to existing vaccines for priming in SARS-CoV-2 naïve individuals. [*not peer reviewed*]
- This study in the United States aimed to evaluate a previously discovered SARS-CoV-2 spike protein stem-helix antibody, CC40.8, for binding to and neutralisation of diverse sarbecoviruses and SARS-CoV-2 Variants of Concern, structurally define and test the protective efficacy of its epitope site. CC40.8 was found to exhibit in vivo protective efficacy against SARS-CoV-2 challenge in two animal models. In both models, CC40.8-treated animals exhibited less weight loss and reduced lung viral titres compared to controls. Their findings can facilitate broadly neutralising antibody (bnAb)-epitope based vaccine development and antibody-based intervention strategies not only to SARS-CoV-2, but against existing human coronaviruses and other coronaviruses that could emerge with pandemic potential.
- This study in China reports on the biochemical characterisation of the Omicron spike trimer and its binding to angiotensin-converting enzyme 2 (ACE2). Their findings reveal that the Omicron receptor binding domain (RBD) was less stable and more dynamic than the wild type RBD, and the Omicron spike trimer has 6-9-fold increased affinity for binding to ACE2. They further describe the structures of the Omicron spike trimer in the apo state, or bound to ACE2 or an anti-Omicron antibody. The ACE2 bound structure revealed that the Omicron spike trimer contains an unusual RBD-RBD interaction and extra interactions in the ACE2-RBD interface, both of which contribute to the higher affinity of ACE2 to the Omicron spike trimer. Structural analysis of the Omicron spike trimer also provides a mechanistic basis for the ability of Omicron to escape most therapeutic antibodies and reduce the efficacy of vaccinations. Their findings open a new venue for antibody drug discovery targeting various strains of SARS-CoV-2, including Omicron.

Vaccines

- The authors in this study conducted in Taiwan developed monovalent receptor-binding domain (RBD)-based mRNA vaccines targeting SARS-COV-2 Omicron and Delta variants. They also tested the concept of bivalent vaccines containing both Delta and Omicron RBD, and a Hybrid vaccine, which combined the mutation sites of Delta and Omicron in single RBD construct. They performed pseudovirus neutralisation assays and found that serum samples from the Omicron vaccinated mice can effectively neutralise Omicron, but not the wild-type (D614G), or other VOCs (Beta and Delta). In contrast, the Omicron/Delta bivalent mRNA vaccine elicited broadly cross-reactive neutralising antibodies, effectively neutralising Omicron and other VOCs. Their results demonstrate that a new generation of multivalent COVID-19 mRNA vaccines is a viable approach to prevent infection from ancestral or VOCs of SARS-CoV-2. [*not peer reviewed*]
- This article presents findings from the final analysis of the multinational, randomised, double-blind, placebo-controlled trial that aimed to assess the efficacy of a single-dose of the viral vector vaccine Ad26.COV2.S (5×10^{10} viral particles). The authors found that a single dose of Ad26.COV2.S provided 52.9% (95% CI, 47.1 to 58.1) protection against moderate to severe–critical COVID-19. Protection varied according to variant; higher protection was observed against severe COVID-19 74.6% (95% CI,

64.7 to 82.1), medical intervention 75.6% (95% CI, 54.3 to 88.0), and death 82.8% (95% CI, 40.5 to 96.8) than against other end points and lasted for 6 months or longer. Ad26.COV2.S was associated with mild-to-moderate adverse events, and no new safety concerns were identified.

- This test-negative, case-control study involving almost 14 million people in Brazil estimated the vaccine effectiveness (VE) of CoronaVac over time and of BNT162b2 booster vaccination against RT–PCR-confirmed SARS-CoV-2 infection and severe COVID-19 outcomes (hospitalisation or death). The authors found that CoronaVac VE at 14–30 days after the second dose was 55.0% (95% CI: 54.3–55.7) against confirmed infection and 82.1% (95% CI: 81.4–82.8) against severe outcomes. VE decreased to 34.7% (95% CI: 33.1–36.2) against infection and 72.5% (95% CI: 70.9–74.0) against severe outcomes over 180 days after the second dose. A BNT162b2 booster, 6 months after the second dose of CoronaVac, improved VE against infection to 92.7% (95% CI: 91.0−94.0) and VE against severe outcomes to 97.3% (95% CI: 96.1−98.1) 14–30 days after the booster. Compared with younger age groups, individuals 80 years of age or older had lower protection after the second dose but similar protection after the booster. Their findings support a BNT162b2 booster vaccine dose after two doses of CoronaVac, particularly for the elderly.
- This prospective cohort study in the U.S characterised the persistence of vaccine-induced maternal anti-S IgG in infant blood and compare persistence of infant anti-S IgG after maternal vaccination vs natural infection. The authors included individuals who had received an mRNA COVID-19 vaccine during pregnancy or were infected with SARS-CoV-2 at 20 to 32 weeks' gestation. They collected matched maternal and umbilical cord serum samples at birth & infant blood at 2 months and 6 months to quantify antibody titres. They found that the majority of infants born to COVID-vaccinated mothers had persistent anti-S antibodies at 6 months, compared with infants born to mothers with SARS-CoV-2 infection. Their findings provide further incentive for pregnant individuals to pursue COVID-19 vaccination.
- This case series examined the association between vaccination coverage and transmission of SARS-CoV-2 at a midsized university in the US. The authors analysed more than 190,000 COVID-19 surveillance tests for 14,894 individuals, including 1,603 positive test results performed from 6th January to 20th May 2021. They found that high vaccination coverage was associated with decreases in numbers of COVID-19 cases within the study population in the campus community. This association was observed with in-person education, congregate living, and the presence of the more transmissible B.1.1.7 (Alpha) variant. Their results support the decision by many colleges and universities to require vaccines and more generally provide evidence of the efficacy of COVID-19 vaccines.
- This population-based cohort study in Israel examined whether BNT162b2 mRNA vaccination during pregnancy is associated with adverse neonatal and early infant outcomes among the new-borns. The authors included 24,288 eligible new-borns of whom 16,697 were exposed (n = 2134 and n = 9364 in the first and second trimesters, respectively) to maternal vaccination in utero. The authors observed no substantial differences in preterm birth rates between exposed and unexposed new-borns or small birth weight for gestational age. No significant differences were observed in the incidence of all-cause neonatal hospitalisations, post neonatal hospitalisations after birth, congenital anomalies, or infant mortality over the study period.
- This test-negative case-control study in England aimed to estimate vaccine effectiveness (VE) against symptomatic COVID-19 and related hospitalisation and death. The authors assessed the effectiveness of the ChAdOx1-S and BNT162b2 vaccines. VE against symptomatic Covid-19 with the delta variant was found to peak in the early weeks after receipt of the 2nd dose and then decreased by 20 weeks to 44.3% (95% CI, 43.2 to 45.4) with the ChAdOx1-S vaccine and to 66.3% (95% CI, 65.7 to 66.9) with the BNT162b2 vaccine. Waning of VE was greater in persons 65 years of age or older than in those 40 to 64 years of age. At 20 weeks or more after vaccination, VE decreased less against both hospitalisation, to 80.0% (95% CI, 76.8 to 82.7) with the ChAdOx1-S vaccine and 91.7% (95% CI, 90.2 to 93.0) with the BNT162b2 vaccine, and death, to 84.8% (95% CI, 76.2 to 90.3) and 91.9% (95% CI, 88.5 to 94.3), respectively. Greater waning in VE against hospitalisation was observed in persons 65 years of age or older in a clinically extremely vulnerable group and in persons 40 to 64 years of age with underlying medical conditions than in healthy adults.

- This retrospective cohort study evaluated the vaccine effectiveness of a third dose of BNT162b2 vaccine in a large United States integrated health system. The authors found that effectiveness waned after receipt of two doses and that being immunised with a third dose of BNT162b2 confered comparable protection against SARS-CoV-2 infections and COVID-19 hospital admissions as was seen in the first few months after receiving two doses. Compared to unvaccinated individuals, receiving a third dose of BNT162b2 was 88% effective (95% CI, 86 to 89) against infections not requiring hospital admission, 90% (95% CI, 88 to 92) against symptomatic COVID-19 not requiring hospital admission, and 97% (95% CI, 95 to 98) against COVID-19-related hospital admissions among all adults aged ≥18 years. The authors recommend further studies to evaluate the effectiveness of the vaccine against the Omicron variant.

Diagnostics

- This systematic review and meta-analysis of 38 studies in the UK aimed to synthesise evidence on the diagnostic accuracy of all known tests for SARS-CoV-2, as well as tests for antibodies to SARS-CoV-2. The authors also systematically summarised evidence on the influence of tissue sample site on virus test detection rates and the influence of test timing relative to disease course on antibody detection. Their results suggest that both these factors could influence test results. They recommend further studies on the performance of point-of-care (near-patient) tests compared with laboratory-based equivalents and with test results in individuals with no or minimal symptoms in community-based settings.
- This article provides a review of New Zealand's COVID-19 test requirements and the collaboration and resources required for producing the reagents needed for the reverse transcription polymerase chain reaction (RT-PCR), and the COVID-19 diagnostic assay referred to as HomeBrew (HB) RT-qPCR from onshore synthesised components. This one-step RT-qPCR assay was evaluated using clinical samples and shown to be comparable to a commercial COVID-19 assay. Through this work the authors demonstrated the expertise and infrastructure capacity to meet reagent supply challenges, if these were to occur in the future.
- The authors in this study developed an up-conversion phosphor technology-based point-of-care testing (UPT-POCT), a lateral flow assay, for rapid COVID-19 diagnosis. The study also predicted seral neutralising antibody (NAb) activity and protective effects. The UPT-POCT was developed targeting total antibodies against the receptor-binding domain (RBD) of SARS-CoV-2 spike protein. They used ELISA as a contrast method and evaluated the quantitation accuracy with Nab and serum samples. The sensitivity and specificity of UPT-POCT were 89.15% and 99.75%, among 782 cases from seven hospitals in China, respectively. The quantitative detection results of UPT-POCT for total antibodies against RBD were significantly correlated with the NAb titres in patients ($r = 0.9404$, n = 527; $\rho = 0.6836$, n = 528) and vaccinated participants ($r = 0.9063$, $\rho = 0.7642$, n = 35), as well as with the protection rate against becoming RP ($r = 0.9886$, n = 312). Their test can be used as a surrogate method for rapid diagnosis and prediction of protective effects.

Care and Treatment

- This multicentre, phase 2-3 double-blind, randomised, controlled trial aimed to evaluate the safety and efficacy of nirmatrelvir plus ritonavir (Paxlovid) in non-hospitalised adults with mild-to-moderate Covid-19 at high risk for progression to severe disease. A total of 2,246 patients were assigned in a 1:1 ratio to receive either 300 mg of nirmatrelvir plus 100 mg of ritonavir or placebo every 12 hours for 5 days. The authors found that the regimen resulted in reductions in the relative risk of hospitalisation for Covid-19 or death from any cause through day 28 of 88.9% and 87.8% among patients commencing treatment within 3 days and within 5 days after symptom onset, respectively. Their findings show that treatment with nirmatrelvir plus ritonavir early in Covid-19 illness can decrease progression to severe disease and quickly reduce SARS-CoV-2 viral load.
- The authors in this study in the UK designed, verified and performed a pre-clinical evaluation of a mechanical ventilator based on components not required for standard ventilators. The UK government had launched a challenge seeking both conventional and novel designs of ventilator systems that could

be manufactured at scale within a few weeks. In response to the challenge, the OxVent ventilator was designed by a team of clinicians and engineers at the University of Oxford and King's College London. The OxVent provides a relatively advanced ventilation support in the form of assisted spontaneous ventilation with production material costs limited to ~ £1,000. The ventilator operated continuously for more than 3 weeks. The design has the potential to be manufactured at large scale and meet demand when a rapid increase in mechanical ventilation capacity is required.

- The authors in this study in Japan conducted live-virus focus reduction neutralisation assays to assess the neutralising activities of monoclonal antibodies (mAbs) against omicron and other variants of concern. They studied both FDA-approved and investigational therapeutic monoclonal antibodies (individually and in combination). They found that all the combinations of mAbs that were tested neutralised the early strain as well as Alpha and Delta variants. The combination of etesevimab plus bamlanivimab showed remarkably reduced neutralising activity against gamma and lost neutralising activity against omicron and beta. The imdevimab–casirivimab combination retained activity against beta and gamma but lost inhibitory capability against omicron. The tixagevimab–cilgavimab combination inhibited beta, gamma, and omicron; however, the $FRNT_{50}$ values of this combination were higher by a factor of 24.8 to 142.9 for omicron than for beta or gamma, respectively. The authors also tested three different antiviral compounds (i.e., remdesivir, molnupiravir, and PF-07304814) for efficacy against Omicron. The efficacy of three compounds against Omicron was similar to the efficacy against the early strain. Their results suggest that all three of these compounds may be efficacious in treating patients infected with the omicron variant.
- This phase 3, double-blind, randomised, placebo-controlled trial aimed to evaluate the efficacy and safety of treatment with molnupiravir. Molnupiravir was started within 5 days after the onset of signs or symptoms in non-hospitalised, unvaccinated adults with mild-to-moderate, laboratory-confirmed Covid-19 and at least one risk factor for severe Covid-19 illness. Participants were randomly assigned to receive 800 mg of molnupiravir or placebo twice daily for 5 days. The authors found that the risk of hospitalisation or death at day 29 was 6.8 percentage points lower (95% CI, −11.3 to −2.4; P=0.001) with molnupiravir than with placebo at the interim analysis and 3.0 percentage points lower (95% CI, −5.9 to −0.1) in the all-randomised analysis, an improvement in an outcome that is potentially meaningful for patients, health care systems, and public health. No safety concerns were detected.

Epidemiology

- This article reports on an investigation of SARS-CoV-2 Delta variant outbreak initially detected in a pet shop worker on 15th January 2022 in Hong Kong. The authors identified the source as pet hamsters imported from the Netherlands. The hamsters were responsible for two independent zoonotic infections in humans and at least one human-to-human transmission event. Their investigation reveals that pet hamsters can acquire SARS-CoV-2 infection in real-life settings and can transmit the virus back to humans. It also suggests that the pet animal trade may be a pathway that can facilitate the movement of SARS-CoV-2 across national borders. [*not peer reviewed*]
- This test-negative, case-control study estimated the effectiveness of previous infection in preventing symptomatic new cases caused by Omicron and other SARS-CoV-2 variants in Qatar. The authors found that the effectiveness of previous infection in preventing reinfection with the alpha, beta, and delta variants of SARS-CoV-2 was robust (at approximately 90%). Such protection against reinfection with the omicron variant was lower 56.0% (95% CI, 50.6 to 60.9) but still considerable. The protection of previous infection against hospitalisation or death caused by reinfection appeared to be robust, regardless of variant. It was estimated to be 69.4% (95% CI, −143.6 to 96.2) against the alpha variant, 88.0% (95% CI, 50.7 to 97.1) against the beta variant, 100% (95% CI, 43.3 to 100) against the delta variant, and 87.8% (95% CI, 47.5 to 97.1) against the omicron variant.
- This retrospective cohort study in the US characterised the risk of persistent and new clinical sequelae in adults aged ≥65 years after the acute phase of SARS-CoV-2 infection. The authors analysed data from the UnitedHealth Group Clinical Research Database. They compared adults with SARS-CoV-2 infection to three different comparison groups (that did not have COVID-19). Their results showed that 32% of adults aged ≥65 years infected with SARS-CoV-2 had a diagnosis of at least one sequela during

the post-acute phase of the illness, 11% higher than in a control group who did not have a diagnosis of COVID-19. The increased risk during the post-acute phase were associated with sequelae related to respiratory, cardiovascular, neurologic, hematologic, endocrine, and kidney systems, and for mental health-related diagnoses. An increased risk for these sequelae was evident among those who were admitted to hospital for COVID-19, but the risk of several sequelae was also increased for men, for those of black race, and for those aged ≥75. Their findings can help to define the sequelae of SARS-CoV-2 infection in the post-acute phase in the older adult population, and to evaluate and manage these patients appropriately.

- This prospective cohort study in the United States examined the characteristics, changes over time, outcomes, and severity risk factors of children with SARS-CoV-2 within the National COVID Cohort Collaborative (N3C). A total of 1,068,410 children were tested for SARS-CoV-2 across 56 sites, of whom, 167,262 (15.6%) had positive test results. The authors observed differences in demographic characteristics, pre-existing comorbidities, and initial vital sign and laboratory values between severity subgroups. Taken together, these results suggest that early identification of children likely to progress to severe disease could be achieved using readily available data elements from the day of admission. Further work is needed to translate this knowledge into improved outcomes.

Infection prevention & control

- This review from Portugal presented a recent and comprehensive demonstration of the state-of-the-art in the use of metals, as well as their mechanisms, to fight different pathogens, such as viruses, bacteria, and fungi. The authors recommend future projects to study dual functionality (involving the combination of biocidal agents with anti-adhesive surfaces) as this approach might be the key to the development of superefficient multifunctional and multimicrobial killing agents.
- This article reviewed the antimicrobial properties of metals such as copper, silver, and zinc along with the effects of combining them with titanium dioxide to create binary or ternary contact-killing surface coatings. The self-cleaning and bacterial resistance of purely structural superhydrophobic surfaces and the potential of physical surface nano protrusions to damage microbial cells are then considered. The authors then provide a detailed discussion on recent advances in attempting to combine these individual phenomena to create super-antimicrobial metal-based coatings with binary or ternary killing potential against a broad range of microorganisms, including SARS-CoV-2. This would be utilised for high-touch surface applications such as hand rails, door plates, and water fittings on public transport and in healthcare, care home and leisure settings as well as personal protective equipment commonly used in hospitals and in the current COVID-19 pandemic.

Non-pharmaceutical interventions, social distancing

- This observational study in São Paulo State, Brazil tested whether reopening schools under appropriate protocols during the COVID-19 pandemic was associated with increased municipal-level COVID-19 cases and deaths. The study included 643 municipalities, of which 129 (20.1%) authorised school re-openings in 2020 (comprising 8,764 schools) and 514 (79.9%) (comprising 9,997 schools) that did not. No statistically significant differences were detected between municipalities that authorised schools to reopen and those that did not for weekly new cases (difference-in-differences, –0.03; 95% CI, –0.09 to 0.03) and weekly new deaths (difference-in-differences, –0.003; 95% CI, –0.011 to 0.004) before and after October 2020. Their results suggest that reopening schools under appropriate protocols in low- and middle-income countries during the pandemic is unlikely to be associated with higher aggregate COVID-19 cases or deaths when counterfactual mobility is already high.
- This cross-sectional study explored patterns on self-reported compliance with six COVID-19 preventive behaviours (mask wearing, hand washing, indoor household mixing, outdoor household mixing, social distancing and compliance with other guidelines) using data from a sample of 20,000 UK adults 8 months after lockdown was first implemented in the UK. The authors further tested whether behavioural patterns were related to a wide range of demographic, socioeconomic and personality trait characteristics. They found evidence that individuals typically display consistent levels of compliance across different preventive behaviours, though average compliance with social distancing was lower

than for other behaviours. Their results suggest that efforts to increase compliance should focus on increasing motivation to comply across all groups and personality traits equally.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 14th February 2022, The Russian Direct Investment Fund (RDIF, Russia's sovereign wealth fund), R-Pharm group and AstraZeneca announced interim results of phase II clinical trials to evaluate the safety and immunogenicity of the combined use of AstraZeneca's vaccine and the first component of the Sputnik V coronavirus vaccine (Sputnik Light). The interim results of the trials, involving 100 volunteers in Russia and 100 volunteers in Azerbaijan. The vaccine combination demonstrated an acceptable safety profile, which is consistent with the results of previous AstraZeneca vaccine, Sputnik V and Sputnik Light vaccine clinical trials. Volunteers were being monitored for 57 days after the first dose. Results demonstrated a good safety profile of the combination. No serious adverse events related to vaccination were registered. Clinical trial registration #: (NCT04684446).
- On 11th February 2022, Pfizer and BioNTech announced plans to extend their rolling submission to the U.S. Food and Drug Administration (FDA) seeking to amend the Emergency Use Authorisation of the Pfizer-BioNTech COVID-19 Vaccine to include children 6 months through 4 years of age, which had been requested by FDA. The announcement was based on the ongoing trial in children 6 months through 4 years of age. Data on the first two 3 µg doses in this age group are being shared with the FDA on an ongoing basis. Phase 1/2/3 trials initially enrolled 4,500 children ages 6 months to under 12 years of age in the United States, Finland, Poland, and Spain from more than 90 clinical trial sites. Additional children have been enrolled in all age groups following study amendments. The trial currently includes approximately 8,300 children. The study was designed to evaluate the safety, tolerability, and immunogenicity of the Pfizer-BioNTech vaccine on a two-dose schedule (approximately 21 days apart) in three age groups: ages 5 to under 12 years; ages 2 to under 5 years; and ages 6 months to under 2 years. Clinical trial registration #: (NCT04816643).
- On 10th February 2022, Novavax announced that NVX-CoV2373 its recombinant nanoparticle protein-based COVID-19 vaccine, achieved its primary effectiveness endpoint in the paediatric expansion of its PREVENT-19 pivotal Phase 3 trial and demonstrated 80% efficacy. The study enrolled 2,247 adolescents aged 12 through 17-years across 73 sites in the U.S. to evaluate safety, effectiveness (immunogenicity), and efficacy, with an emphasis on ensuring well balanced racial and ethnic representation among participants. Trial demonstrated 82% clinical efficacy against Delta variant, immune responses were about two-to-three-fold higher in adolescents than in adults against all variants studied. Vaccine was well-tolerated with no safety signals identified. Clinical trial registration #: (NCT04611802).

Therapeutics trials:

- On 16th February 2022, Enanta Pharmaceuticals announced that it has dosed the first subject in its Phase 1 clinical trial of EDP-235, a coronavirus 3CL protease inhibitor (Mpro) specifically designed as a once-daily, oral treatment for COVID-19. This first-in-human Phase 1 study will evaluate the safety, tolerability, and pharmacokinetics of oral EDP-235 in single ascending doses (SAD) and multiple ascending doses (MAD) compared to placebo in healthy volunteers. All SAD and MAD cohorts will enrol eight participants who will be randomised to receive EDP-235 or placebo in a 3:1 ratio. Preclinical data show that EDP-235 potently blocks the replication of SARS-CoV-2 in multiple cellular models, including primary human airway epithelial cells where an EC90 of 33 nanomolar was observed. EDP-235 demonstrates a good oral bioavailability without ritonavir boosting and favourable distribution into lung cells as well as other key target tissues.
- On 14th February 2022, Arch Biopartners announced that Health Canada has approved the amendment to the CATCO protocol to include its lead drug candidate, LSALT Peptide (LSALT and "Metablok") in a

new dosing arm of the trial. CATCO is a multi-centre, adaptive, randomised, open-label, controlled study being conducted in up to fifty-five hospitals across Canada to find new treatments for patients suffering from the complications caused by COVID-19. LSALT Peptide (LSALT) is a novel drug candidate that targets acute organ inflammation in the lungs, liver and kidneys common in several indications, including moderate to severe cases of COVID-19, regardless of variant type. Clinical trial registration #: (NCT04330690).

- On 11th February 2022, Kintor Pharmaceutical announced the enrolment and dosing of first patient in China at Third People's Hospital of Shenzhen in its multi-regional phase III clinical trial of proxalutamide for the treatment of COVID-19 outpatients. Proxalutamide is a nonsteroidal antiandrogen targeting AR-ACE2/TMPRSS2 signal axis which significantly inhibit the entry of the virus into host cells by transcriptionally down-regulating the expression of TMRPSS2 and ACE2. Its mechanism of action reduces the intensity of the cytokine response by activating the Nrf2 pathway, which inhibits the over production of IL-6, proinflammatory cytokines, and chemokines. The phase III trial was designed as a randomised, double-blind, placebo-controlled, multi-regional study, designed to evaluate the efficacy and safety of proxalutamide in male COVID-19 outpatients. The study has enrolled nearly 200 patients from various countries including China, Brazil, Philippines and Malaysia. Clinical trial registration #: (NCT04869228).
- On 11th February 2022, Roche announced Actemra/RoActemra (tocilizumab) intravenous (IV) has been granted World Health Organization (WHO) prequalification for the treatment of COVID-19 in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation. Actemra/RoActemra is a first-in-class anti-interleukin-6 receptor (aIL-6R) therapy which besides treating severe and critical COVID 19 it is also a treatment of rheumatoid arthritis, systemic juvenile idiopathic arthritis, polyarticular juvenile idiopathic arthritis, giant cell arteritis and chimeric antigen receptor T-cell induced severe or life-threatening cytokine release syndrome. Multiple studies have evaluated the efficacy and safety of Actemra/RoActemra, including the Roche-led COVACTA, EMPACTA and REMDACTA trials, and the University of Oxford-led RECOVERY study. These studies support Actemra/RoActemra as a high quality, safe and efficacious treatment for severe and critical COVID-19 adults.
- On 11th February 2022, Gilead Sciences announced new data from an interim analysis of its ongoing, Phase 2/3 single arm, open-label study to evaluate the safety, tolerability and pharmacokinetics of Veklury (remdesivir) in paediatric patients aged from 28 days to less than 18 years hospitalised with COVID-19. Overall, a total of 53 paediatric patients were enrolled, no new safety signals were apparent for Veklury. Overall, 38 patients (72%) experienced adverse events (AEs), with 11 patients (21%) experiencing serious adverse events (SAEs) that were determined not to be study-drug related. Majority (85%) had clinical improvement based on the clinical ordinal scale and the recovery rate was 83% at last assessment. Most common adverse events were constipation (17%), acute kidney injury (11%), hyperglycaemia (9%), pyrexia (9%) and increased alanine transaminase (ALT) (8%). Veklury was generally well tolerated with a high proportion of participants showing clinical improvement and recovery. Clinical trial registration #: (NCT04431453).
- On 10th February 2022, Molecular Partners announced that Novartis has requested Emergency Use Authorisation (EUA) from the U.S. Food and Drug Administration (FDA) for ensovibep, a DARPin antiviral therapeutic candidate to treat COVID-19. Ensovibep is a Designed Ankyrin Repeat Proteins (DARPin) therapeutic candidate, designed specifically to inhibit target cell entry of SARS-CoV-2. The treatment is designed to block the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein, even in the presence of multiple mutations in the spike protein. The submission is based on the totality of the data from clinical and preclinical studies including the positive results of the Phase 2 portion of the EMPATHY study, a randomised, placebo-controlled study which enrolled 407 symptomatic patients infected with SARS-Cov-2. Clinical trial registration #: (NCT04828161).

- On 7th February 2022, RedHill announced results from two recently completed prespecified analyses from the oral opaganib Phase 2/3 study in hospitalised severe COVID-19 patients. Opaganib, a new chemical entity, is a proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor, with proposed dual anti-inflammatory and antiviral activity. Results revealed opaganib significantly reduced mortality when given to patients who received remdesivir and corticosteroids, the best available standard-of-care (SoC) for hospitalised COVID 19 patients. The treatment demonstrated a significant 70.2% mortality benefit for opaganib treated patients, with a mortality rate of 6.98% (n=3/43) for the opaganib arm + SoC versus 23.4% (n=11/47) for placebo + SoC by Day 42 (p value=0.034). Opaganib delivered a significant 34% benefit in time to recovery by day 14 with 37.4% of opaganib-treated patients (n=86/230) reaching this event versus 27.9% of patients (n=65/233) treated with placebo + SoC (p value=0.013). The safety and tolerability profile of the interventional arm was similar to placebo. Clinical trial registration #: (NCT04467840).
- On 3rd February 2022, Pardes Biosciences announced that its Investigational New Drug (IND) application for PBI-0451 has been cleared by the United States Food and Drug Administration (FDA) to treat and prevent COVID-19. PBI-0451 is an investigational orally bioavailable direct-acting antiviral (DAA) inhibitor of the main protease (Mpro), an essential protein required for the replication of coronaviruses, including the novel SARS-CoV-2 that causes COVID-19. PBI-0451 is currently in a Phase 1 placebo-controlled, blinded, randomised, dose escalation study in healthy volunteers in New Zealand evaluating the safety, tolerability, and pharmacokinetics after single and multiple ascending doses. Additional Phase 1 clinical trials for PBI-0451 in the U.S. is at initiation stage. Clinical trial registration #: (NCT05011812).

Immunotherapies trials:

- On 11th February 2022, Eli Lilly announced that the U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorisation (EUA) for bebtelovimab, an antibody that demonstrates neutralisation against the Omicron variant. Bebtelovimab can now be used for the treatment of mild-to-moderate COVID-19 in adults and paediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalisation or death. The authorised dose of bebtelovimab is 175 mg given as an intravenous injection over at least 30 seconds. The EUA is based on data analyses from the Phase 2 BLAZE-4 trial, treatment arms 9-14. The trial aimed to evaluate treatment of non-hospitalised patients with mild-to-moderate COVID-19 treated with the authorised dose of bebtelovimab (175 mg) alone or together with 700 mg bamlanivimab and 1,400 mg of etesevimab. Pseudo virus and authentic virus testing demonstrate that bebtelovimab retains full neutralising activity against all other known variants of interest and concern, including Omicron. Clinical trial registration #: (NCT04634409).
- On 9th February 2022, IGM Biosciences announced its progress in two Phase 1 clinical trials evaluating IGM-6268, an anti-SARS-CoV-2 IgM monoclonal antibody, for the treatment and prevention of mild to moderate COVID-19. IGM-6268 is an engineered IgM antibody that specifically targets the receptor binding domain (RBD) of the SARS-CoV-2 spike protein. It has 10 binding sites to the spike protein administered by intranasal plus intraoral spray once for 1 day (SAD), or once or twice each day for 5 days (MAD). The primary mechanism of action of IGM-6268 is to block the binding of the SARS-CoV-2 RBD on the spike protein to human angiotensin converting enzyme 2 (hACE2), the cellular receptor for SARS-CoV-2 and hence neutralises the infectivity of the virus. In vitro studies indicate IGM-6268 exhibits potent neutralisation activity against the Omicron and Delta variants and all other Variants of Concern and Variants of Interest. A phase 1 clinical trial in the U.S., is a multi-centre, randomised, double-blinded, placebo-controlled single (SAD) and multiple (MAD) ascending dose study to assess the safety, tolerability, and pharmacokinetics of IGM-6268 administered intranasally in healthy volunteers in U.S and South Africa. A phase 1a/1b clinical trial in South Africa, is a multi-centre,

randomised, double-blinded, placebo-controlled study to assess the safety, tolerability, pharmacokinetics, and preliminary efficacy of IGM-6268. Clinical trial registration #: (NCT05184218).

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

Contributors

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