

# COVID-19 Scientific and Public Health Policy Update<sup>1</sup>

## (30 March 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. It 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 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. 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

**749.8 Million**

Vaccines Supplied

**502.4 Million**

Vaccines Administered

### African Population Vaccinated

**20.5%**

Partially Vaccinated

**15.6%**

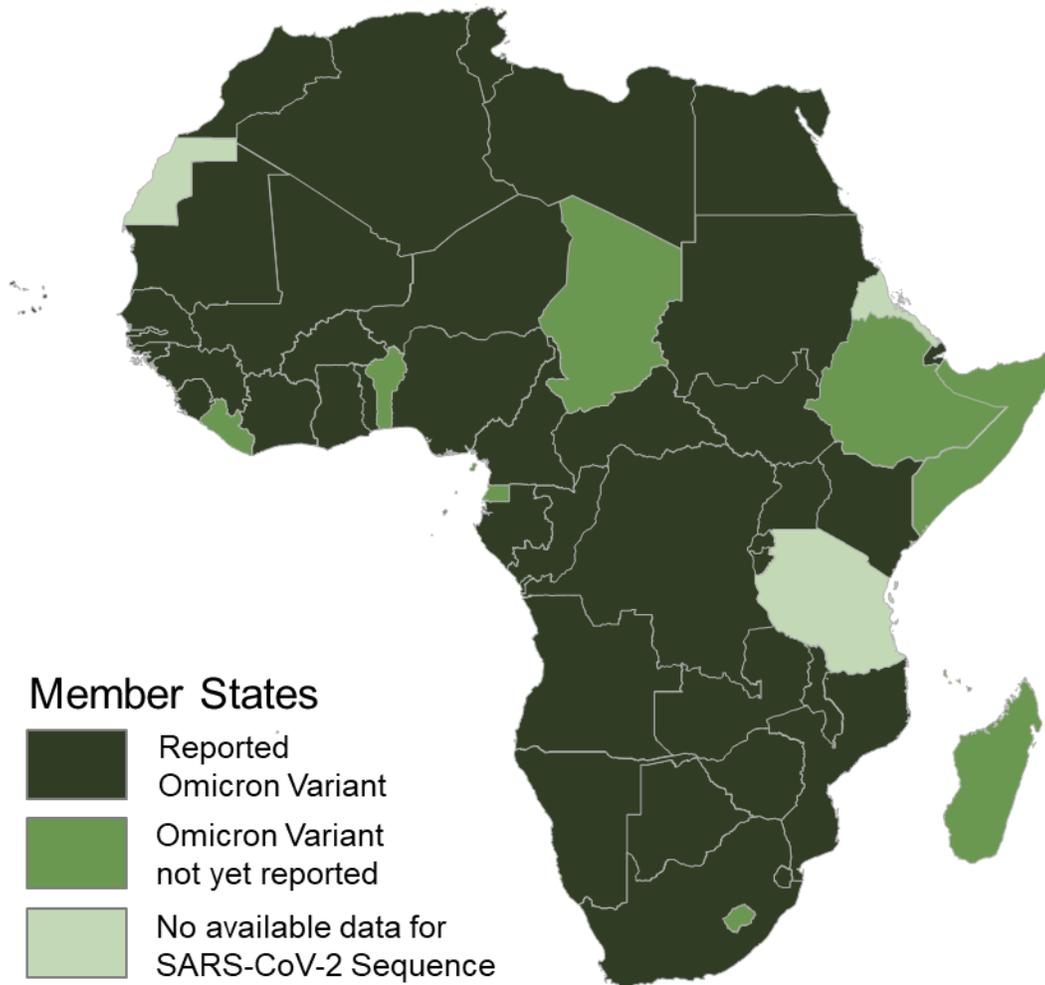
Fully Vaccinated\*

\*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 30<sup>th</sup> March, 2022

<sup>1</sup> 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 24<sup>th</sup> November 2021, has spread to 198 countries/territories/areas worldwide. As of 30 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 30<sup>th</sup> March, 2022

### B. New guidelines and resources

Since 15<sup>th</sup> March 2022,

- Africa CDC<sup>2</sup> has published new guidance and resources on:
  - [Outbreak Brief 114: Coronavirus Disease 2019 \(COVID-19\) Pandemic](#)
- U.S. CDC<sup>3</sup> has published new guidance and resources on:
  - [Guidance for Reporting SARS-CoV-2 Sequencing Results](#)
- WHO<sup>4</sup> has published new guidance and resources on:

<sup>2</sup> Africa CDC: Africa Centres for Disease Control and Prevention

<sup>3</sup> U.S. CDC: United States Centers for Disease Control and Prevention

<sup>4</sup> WHO: World Health Organization

- [Global genomic surveillance strategy for pathogens with pandemic and epidemic potential, 2022–2032](#)
- [Global workshop on enhancing sequencing to monitor SARS-CoV-2 evolution: report of a virtual meeting](#)
- [Interim recommendations for use of the inactivated COVID-19 vaccine, CoronaVac, developed by Sinovac](#)
- [Interim recommendations for use of the inactivated COVID-19 vaccine BIBP developed by China National Biotec Group \(CNBG\), Sinopharm](#)
- [Interim recommendations for use of the Bharat Biotech BBV152 COVAXIN® vaccine against COVID-19](#)
- U.S. FDA<sup>5</sup> has issued press releases on:
  - [On 29<sup>th</sup> March, FDA Authorises Second Booster Dose of Two COVID-19 Vaccines for Older and Immunocompromised Individuals](#)
  - [On 25<sup>th</sup> March, FDA announced the COVID-19 treatment sotrovimab is no longer authorized for use at this time in the U.S. Health and Human Services \(HHS\) regions 1 and 2 due to the high frequency of the Omicron BA.2 sub-variant](#)
  - [On 16<sup>th</sup> March, the FDA issued an emergency use authorisation for PHASE Scientific International, Ltd.'s INDICAID COVID-19 Rapid Antigen At-Home Test](#)
  - [As of 29<sup>th</sup> March, 425 tests and sample collection devices are authorised by the FDA under emergency use authorisations](#)
- ECDC<sup>6</sup> has issued new resources on:
  - [Guidance for the prevention and control of COVID-19 in temporary reception centres in the context of the large numbers of people fleeing Ukraine](#)
  - [Analysis of COVID-19 contact tracing data from Ireland, Italy and Spain – 2020 data](#)
- UKHSA<sup>7</sup> has issued new guidance and press releases on:
  - [COVID-19: adult surveillance](#)
  - [National protocol for COVID-19 Vaccine AstraZeneca \(ChAdOx1-S \[recombinant\]\)](#)
  - [National protocol for Comirnaty® 30microgram/dose COVID-19 mRNA vaccine](#)
  - [National protocol for Spikevax \(formerly COVID-19 Vaccine Moderna\)](#)
  - [COVID-19 vaccination: British Sign Language resources](#)

## Scientific updates

### Basic Science

- This [case report](#) from the United States presents a 70-year-old woman with Stage IV Non-Hodgkin's lymphoma (NHL) who developed an indolent, protracted course of SARS-CoV-2 infection. Remdesivir therapy alleviated symptoms and produced a transient virologic response, but her course was complicated by recrudescence of high-grade viral shedding. Whole genome sequencing identified a mutation, E802D, in the nsp12 RNA-dependent RNA polymerase, which was not present in pre-treatment specimens. In vitro experiments demonstrated that the mutation conferred a ~6-fold increase in remdesivir IC<sub>50</sub> but resulted in a fitness cost in the absence of remdesivir. Sustained clinical and virologic response was achieved after treatment with casirivimab-imdevimab. Their findings illustrate the importance of monitoring for remdesivir resistance and the potential benefit of combinatorial therapies in immunocompromised patients with SARS-CoV-2 infection.
- This [study](#) in Germany analysed fetal magnetic resonance imaging (MRI) data from 34 pregnant women with mild symptoms of PCR-proven SARS-CoV-2 infection. Lung volume was assessed as a measure of pulmonary fetal lung growth. Normalised fetal lung volume was significantly reduced

<sup>5</sup> U.S. FDA: United States Food and Drug Administration

<sup>6</sup> ECDC: European Centre for Disease Prevention and Control

<sup>7</sup> UKHSA: United Kingdom Health Security Agency

compared with age-adjusted reference values, in the absence of structural abnormalities or organ infarction, and was unexplained by differences in somatic growth (84% vs 24% of 50th percentile reference;  $p < 0.0001$ ). The timepoint of infection showed significant effects on fetal lung growth, with reduced lung volumes observed with SARS-CoV-2 infections acquired during the third trimester (69% vs 91% of 50th percentile reference in the first or second trimester;  $p = 0.0249$ ).

- This [retrospective study](#) in Austria performed neutralisation assays against six SARS-CoV-2 variants in serum samples obtained from persons who had recovered from infection with the Omicron BA.1 variant, with or without preexisting SARS-CoV-2 immunity. They found that neutralising antibody (nAb) titers against all the variants were high among vaccinated persons after Omicron BA.1 breakthrough infection and among vaccinated or unvaccinated persons who had previous infection with the wild-type, Alpha, or Delta variant before infection with Omicron BA.1. Mean nAb titers against the Omicron BA.1 variant were lower than those against the other variants among previously vaccinated persons but were similar to those against the other variants among unvaccinated persons who had had infection with the wild-type, alpha, or delta variant before infection with the omicron BA.1 variant. In contrast, samples obtained from unvaccinated persons who had not had previous SARS-CoV-2 infection before infection with the omicron BA.1 variant contained mainly nAbs against omicron BA.1 and only occasionally contained nAbs against the other variants. These findings support the hypothesis that omicron BA.1 is an extremely potent immune-escape variant, showing limited cross-reactivity with earlier variants.

### Vaccines

- This [prospective cohort study](#) in Malawi assessed the dynamics of anti-Spike antibodies in 52 adults with prior SARS-CoV-2 infection and determined the effect of subsequent COVID-19 vaccination with ChAdOx nCov-19 in 12 of these adults. The patients were recruited during the first two epidemic waves and followed up every 30 days for a maximum of 270 days. They found that antibody pseudovirus neutralisation activity following SARS-CoV-2 infection wanes within 6 months post laboratory-confirmed diagnosis of mild/moderate COVID-19 (30–60 days vs. 210–270 days; Log ID<sub>50</sub> 6.8 vs. 5.3,  $p = 0.0093$ ). High concentrations of binding anti-Spike and anti-RBD IgG antibodies were associated with the presence of pseudovirus neutralisation activity in convalescent serum ( $p < 0.0001$ ). Vaccination with a single dose of the AstraZeneca COVID-19 vaccine following mild/moderate SARS-CoV-2 infection induced a 2 to 3-fold increase in anti-Spike and -RBD IgG levels 30 days post-vaccination (both,  $p < 0.0001$ ). The anti-RBD IgG antibodies from these vaccinated individuals were broadly cross-reactive against multiple variants of concern and had neutralisation potency against original D614G, beta, and delta variants.
- This [cohort study](#) in the United States assessed the association between receiving the Ad26.COV2.S vaccine and COVID-19-related infections and hospitalisations before and during the Delta variant surge. The study included 422,034 vaccinated and 1,645,397 unvaccinated adults matched by date, location, age, sex, and comorbidity index. Vaccine effectiveness (VE) was estimated to be 76% (95% CI, 75%-77%) for COVID-19 infection and 81% (95% CI, 78%-82%) for COVID-19-related hospitalisation for at least 180 days after vaccination before and during the Delta variant surge. VE for COVID-19 infection was higher in patients younger than 65 years (VE=78%; 95% CI, 77%-79%) and lower in immunocompromised patients (VE=64%; 95% CI, 59%-68%).
- This [cohort study](#) in Singapore compared the incidence rates and clinical characteristics of cerebral venous thrombosis (CVT) following either SARS-CoV-2 infection or mRNA-based SARS-CoV-2 vaccination. The study involved 62,447 individuals with SARS-CoV-2 infection and 3,006,662 individuals who received mRNA-based SARS-CoV-2 vaccines (BNT162b2 or mRNA-1273). The authors identified 6 and 9 CVT cases in the SARS-CoV-2 and vaccine groups, respectively. The crude incidence rate (IR) of CVT after SARS-CoV-2 infections was 83.3 per 100 000 person-years (95% CI, 30.6-181.2 per 100 000 person-years) and 2.59 per 100 000 person-years (95% CI, 1.19-4.92 per 100 000 person-years) after mRNA-based SARS-CoV-2 vaccination. Six (66.7%) received BNT162b2 vaccine and 3 (33.3%) received mRNA-1273 vaccine. The crude incidence rate ratio (IRR) of CVT hospitalisations with SARS-CoV-2 infection compared with those who received mRNA SARS-CoV-2 vaccination was 32.1 (95% CI, 9.40-101;  $p < .001$ ). These findings suggest that the risk of CVT after SARS-CoV-2 infection is higher than after mRNA-based SARS-CoV-2 vaccination.

- This [population-based retrospective cohort study](#) in Canada evaluated the peripartum outcomes following COVID-19 vaccination during pregnancy. Among 97,590 individuals (mean [SD] age, 31.9 [4.9] years), 22,660 (23%) received at least 1 dose of COVID-19 vaccine during pregnancy (63.6% received dose 1 in the third trimester; 99.8% received an mRNA vaccine). Compared with vaccination after pregnancy and remaining unvaccinated, COVID-19 vaccination during pregnancy was not significantly associated with increased risk of postpartum hemorrhage (incidence: 3.0% vs 3.0%; aRR, 0.91 [95% CI, 0.82-1.02]), chorioamnionitis (0.5% vs 0.5%; aRR, 0.92 [95% CI, 0.70-1.21]), cesarean delivery (30.8% vs 32.2%; aRR, 0.92 [95% CI, 0.89-0.95]), neonatal intensive care unit admission (11.0% vs 13.3%; aRR, 0.85 [95% CI, 0.80-0.90]), or low Apgar score (1.8% vs 2.0%; aRR, 0.84 [95% CI, 0.73-0.97]).

#### Diagnosics

- This [retrospective comparative effectiveness study](#) in the United States assessed the performance of an employee screening program using single vs repeated antigen tests compared with RT-qPCR among asymptomatic individuals. A total of 179,127 rapid SARS-CoV-2 antigen tests were performed, with a 0.35% positivity rate. Of 623 total positive test results, 238 (38%) were confirmed to be true positive and 385 (62%) false positive by RT-qPCR. Of the 623 tests with positive results, 569 (91%) were followed by a second rapid antigen test. Of 224 sets of tests with concordant results, RT-qPCR results were positive for 207 (92%). When the result of the first antigen test was positive and the result of the second antigen test was negative (n = 345), RT-qPCR results were negative for 328 (95%). The overall estimated accuracy of a second antigen test was 94%. These findings may have important implications for how rapid antigen tests can be deployed for more accurate results, especially in a setting where the time to results is important and where widespread PCR testing may be cost prohibitive.

#### Care and Treatment

- This [randomised clinical trial](#) across 57 sites in Brazil, Canada, Peru, Spain, and the United States of America evaluated the efficacy and adverse events of sotrovimab in preventing progression of mild to moderate COVID-19 to severe disease. The study enrolled 1,057 participants who were randomised (1:1) to receive an intravenous infusion with 500 mg of sotrovimab (n = 528) or a placebo (n = 529). All-cause hospitalisation lasting longer than 24 hours or death was significantly reduced following the infusion of sotrovimab (6/528 [1%]) vs placebo (30/529 [6%]) (adjusted relative risk [RR], 0.21 [95% CI, 0.09 to 0.50]; absolute difference, -4.53% [95% CI, -6.70% to -2.37%];  $p < .001$ ). Four of the 5 secondary outcomes were statistically significant in favor of sotrovimab, including reduced emergency department visits, hospitalisation, progression to severe or critical respiratory COVID-19, and death.
- This [blinded, placebo-controlled randomised clinical trial](#) in the United States assessed the efficacy of losartan on lung injury in hospitalised patients with COVID-19. The study enrolled 205 patients across 13 hospitals. Patients were assigned to receive losartan 50 mg (n=101) orally twice daily or placebo (n=104) for 10 days or until hospital discharge. The primary outcome was the imputed arterial partial pressure of oxygen to fraction of inspired oxygen (PaO<sub>2</sub>:FiO<sub>2</sub>) ratio at 7 days. Compared with placebo, losartan did not significantly affect PaO<sub>2</sub>:FiO<sub>2</sub> ratio at 7 days (difference, -24.8 [95%, -55.6 to 6.1];  $p = .12$ ). Secondary outcomes, including ventilator-free days and mortality, were unaffected. However, patients treated with losartan had fewer vasopressor-free days than placebo (median [IQR], 9.4 [9.1-9.8] vasopressor-free days vs 8.7 [8.2-9.3] vasopressor-free days). These findings may have implications for ongoing clinical trials.
- This [meta-analysis](#) of 12 randomised clinical trials evaluated the association between regional prevalence of strongyloidiasis and ivermectin trial results for the outcome of COVID-19 mortality. A total of 3,901 patients were included in the analysis. Four trials (33%) took place in regions of high strongyloidiasis prevalence and 8 (67%) trials took place in regions of low strongyloidiasis prevalence. Ivermectin trials that took place in areas of high regional strongyloidiasis prevalence were associated with a significantly decreased relative risk of mortality (RR, 0.25 [95% CI, 0.09-0.70];  $p = .008$ ). The meta-regression analysis revealed an RR decrease of 38.83% (95% CI, 0.87%-62.25%) for each 5% increase in strongyloidiasis prevalence. These findings suggest that strongyloidiasis prevalence interacts with the relative risk of mortality in ivermectin trial results. No evidence was found to support

the role of ivermectin in preventing mortality in patients with COVID-19 in regions where strongyloidiasis is not endemic.

- This [cohort study](#) in the United States assessed whether early aspirin use is associated with lower risk of in-hospital mortality in patients with moderate COVID-19 compared to patients who did not receive aspirin. The study involved 112,269 hospitalised patients with moderate COVID-19 across 64 health systems. The overall in-hospital mortality was 10.9%. The 28-day in-hospital mortality was significantly lower in those who received aspirin (odds ratio [OR], 0.85; 95% CI, 0.79-0.92). The rate of pulmonary embolism was also significantly lower in patients who received aspirin (OR, 0.71; 95% CI, 0.56-0.90). The benefit was greatest among patients older than 60 years (61-80 years: OR, 0.79; 95% CI, 0.72-0.87; and >80 years: OR, 0.79; 95% CI, 0.69-0.91) and patients with comorbidities (1 comorbidity: OR, 0.68; 95% CI, 0.55-0.83; 2 comorbidities: OR, 0.80; 95% CI, 0.69-0.93; 3 comorbidities: OR, 0.78; 95% CI, 0.68-0.89; >3 comorbidities; OR, 0.74; 95% CI, 0.66-0.84).
- This [case report](#) from the United States presents a 48-year-old African American male who was diagnosed with Graves' disease (hyperthyroidism) after being admitted to the hospital for complaints of cough, fatigue, and palpitations. He tested positive for SARS-CoV-2 and was found to have suppressed thyroid-stimulating hormone (TSH) and an elevated free T4. The patient had no prior history of thyroid disease. The patient was initially diagnosed with viral thyroiditis and was discharged with a prescription of prednisone. However, he was found to have positive thyroid-stimulating immunoglobulin (TSI) and a diffuse increase in flow on doppler ultrasound of the thyroid. Subsequently, the patient was started on anti-thyroid medications with significant improvement. This case may alert clinicians to think of the possibility of SARS-CoV-2-induced autoimmune hyperthyroidism in patients presenting with hyperthyroidism post-COVID.

## Epidemiology

- This [cross-sectional study](#) in South Africa estimated the prevalence of long COVID in mild COVID-19 patients, documented the impact of COVID-19 on 174 patients' well-being, work, and access to long COVID treatment. The authors found that 60% of patients with mild COVID-19 had  $\geq 1$  long COVID symptom, while 35% had  $\geq 3$  ongoing symptoms for two months. Fatigue (35%) and dyspnoea (20%) were the most common symptoms. The findings revealed that 52% of employed patients missed work and 25% of patients self-reported non-recovery from their COVID-19 infection. Moreover, 24% of patients consulted a clinician for long COVID, but only 7% of patients received long COVID care in the public sector. The findings suggest that there is a great need for long COVID treatment in public healthcare services.
- This [population-based cohort study](#) of 43,886 pregnant women in the United States assessed the risk of perinatal complications associated with SARS-CoV-2 infection and described factors associated with hospitalisation. Individuals with SARS-CoV-2 infection had higher risk for severe maternal morbidity (hazard ratio [HR], 2.45; 95% CI, 1.91-3.13), preterm birth (<37 weeks; HR, 2.08; 95% CI, 1.75-2.47), and venous thromboembolism (HR, 3.08; 95% CI, 1.09-8.74) than pregnant women without SARS-CoV-2 after adjusting for demographic characteristics, comorbidities, and smoking status. SARS-CoV-2 infection was also associated with increased risk of medically indicated preterm birth (HR, 2.56; 95% CI, 2.06-3.19); spontaneous preterm birth (HR, 1.61; 95% CI, 1.22-2.13); and early (HR, 2.52; 95% CI, 1.49-4.24), moderate (HR, 2.18; 95% CI, 1.25-3.80), and late (HR, 1.95; 95% CI, 1.61-2.37) preterm birth. The findings inform clinicians and patients about the risk of perinatal complications associated with SARS-CoV-2 infection in pregnancy and support vaccination of pregnant women and those planning conception.
- This [retrospective cohort study](#) in Sweden and Norway assessed the risk of adverse pregnancy outcomes after vaccination against SARS-CoV-2 during pregnancy. The study involved 157,521 singleton pregnancies from 1 January, 2021, until 12 January, 2022 (Sweden), or 15 January, 2022 (Norway). A total of 0.7%, 8.3%, and 9.1% of women were vaccinated during the first, second, and third trimester, respectively. Compared with an unvaccination status, vaccination against SARS-CoV-2 during pregnancy was not significantly associated with increased risk of preterm birth (adjusted

hazard ratio [aHR], 0.98), stillbirth (aHR, 0.86), small for gestational age (adjusted odds ratio [aOR], 0.97), low Apgar score (aOR, 0.97), or neonatal care admission (aOR, 0.97). The findings suggest that COVID-19 vaccination can be safely provided to pregnant women during the second and third trimesters of pregnancy.

- This [decision analytic modelling study](#) in South Korea assessed the association of age and susceptibility to the Delta variant of SARS-CoV-2. The study analysed data obtained from 106,866 confirmed COVID-19 patients. A significant difference in age-specific susceptibility to the Delta vs pre-Delta variant was found in the younger age group. After adjusting for social contact patterns and vaccination status, the increase in susceptibility to the Delta vs pre-Delta variant was estimated to be highest in patients aged 10 to 15 years, approximately doubling (1.92-fold increase [95% CI, 1.86-fold to 1.98-fold]), whereas in patients aged 50 years or more, susceptibility to the Delta vs pre-Delta variant remained stable at an approximately 1-fold change (eg, among individuals aged 50-55 years: 0.997-fold [95% CI, 0.989-fold to 1.001-fold]). The Delta variant of SARS-CoV-2 was estimated to propagate more easily among children and adolescents than pre-Delta strains, even after adjusting for social contact patterns and vaccination status.
- This [cross-sectional study](#) in Japan evaluated the robustness of statistically significant findings from 47 randomised clinical trials (RCTs) for COVID-19 using the fragility index (i.e, the minimum number of participants who would need to have had a different outcome for the RCT to lose statistical significance). Of the 47 RCTs for COVID-19 included, 36 (77%) were studies of the effects of treatment drugs, 5 (11%) were studies of vaccines, and 6 (13%) were of other interventions. A total of 138,235 participants were included in these trials. The median (Interquartile range [IQR]) fragility index of the included trials was 4 (1-11). The medians (IQRs) of the fragility indexes of RCTs of treatment drugs, vaccines, and other interventions were 2.5 (1-6), 119 (61-139), and 4.5 (1-18), respectively. These findings suggest that health care professionals and policy makers should not rely heavily on individual results of RCTs for COVID-19.
- This [case-control study](#) in Denmark investigated cognitive impairment, neuropsychiatric diagnoses, and symptoms in survivors of COVID-19 compared with patients hospitalised for non-COVID-19 illness. The study involved 85 COVID-19 survivors and 61 control patients with non-COVID-19 illness matched for age, sex, and intensive care unit admission status. Cognitive status measured by total geometric mean Montreal Cognitive Assessment (MoCA) scores at 6-month follow-up were lower ( $p = .01$ ) among COVID-19 survivors (26.7; 95% CI, 26.2-27.1) than control patients (27.5; 95% CI, 27.0-27.9). The cognitive status improved substantially ( $p = .004$ ), from 19.2 (95% CI, 15.2-23.2) at discharge to 26.1 (95% CI, 23.1-29.1) for 15 patients with COVID-19 with MoCA evaluations from hospital discharge. COVID-19 (19%) and control patients (20%) had a statistically similar risk of new-onset psychiatric diagnosis at 6-month follow-up (Odds Ratio, OR = 0.93; 95% CI, 0.39-2.27;  $p = .87$ ).

### Infection prevention & control

- This [review](#) from South Africa presents a synopsis of the global mismanagement of personal protective equipment (PPE) waste and highlights the devastating ramifications of the ensuing environment. The review describe the negative impact of PPE litter on environmental systems on varying levels around the globe. Furthermore, peak plastic loads are transported by Asian rivers and are deposited into the Pacific and Indian Oceans. Beaches and seabed are the major sinks of COVID-19 PPE litter, making benthic organisms to be the most vulnerable. The authors recommend further studies to monitor the impact of COVID-19 PPE litter on the environment and aquatic resources.
- This [review](#) article from Bulgaria presents alternative pharmaceutical products individuals can use to provide self-protection against respiratory infections. The authors present contemporary methods of immune- and chemoprophylaxis and their suitability and applicability of these methods in topical mucosal dosage forms for SARS-CoV-2 prophylaxis.

### Non-pharmaceutical interventions, social distancing

- This [decision analytical modelling study](#) in the United States estimated the number of COVID-19 cases and hospitalisations averted nationwide by states' case investigation and contact tracing (CICT) programs. The study used CICT program data from 23 jurisdictions and estimated that 1.11 million cases and 27,231 hospitalisations were averted under a scenario where 80% of interviewed cases and monitored contacts and 30% of notified contacts fully complied with isolation and quarantine guidance, eliminating their contributions to future transmission. As many as 1.36 million cases and 33,527 hospitalisations could have been prevented if all interviewed cases and monitored contacts had entered into and fully complied with isolation and quarantine guidelines upon being interviewed or notified. Across both scenarios and all jurisdictions, CICT averted an estimated median of 21.2% (range, 1.3%-65.8%) of the cases not prevented by vaccination and other nonpharmaceutical interventions.

## D. Clinical Trials Updates

### Key updates:

#### Vaccine trials:

- On 28<sup>th</sup> March 2022, [Vaxxinity announced initial dosing participants in a Phase 3 pivotal trial of UB-612, the COVID-19 booster candidate](#). UB-612 is the first multipeptide subunit protein/peptide-based vaccine candidate for SARS-CoV-2, which is designed to activate both B and T-cell arms of the immune system. Phase 1 and Phase 2 trials of UB-612 conducted in ~4000 participants have shown UB-612 to be well tolerated with no vaccine-related serious adverse events. The most striking findings were induction of long lasting virus neutralising antibodies, broad T-cell immunity against SARS-CoV-2 variants and a strong booster memory recall inducing high levels of neutralising antibodies against Delta and Omicron variants. The pivotal, head-to-head Phase 3 heterologous booster trial will evaluate the potential for UB-612 to boost immunity against COVID-19 in people who have been fully vaccinated with an mRNA (BNT162b2), adenovirus vector (ChAdOx1-S), or inactivated virus (Sinopharm BIBP) COVID-19 vaccine. The primary objective of this active-controlled, randomised, multicenter study is to determine non-inferiority of UB-612-stimulated neutralising antibodies versus the three comparator vaccines. Additionally, neutralising antibodies against Omicron and other variants, non-neutralising functional antibodies and T cell responses will be analyzed as part of secondary and exploratory objectives. Clinical trial registration #: (NCT05293665)
- On 25<sup>th</sup> March 2022, [Novavax announced that its protein-based COVID-19 vaccine, NVX-CoV2373 is included in two trials to evaluate the safety, immunogenicity, and reactogenicity of the vaccine as a booster amidst the ongoing COVID-19 pandemic](#). Both trials have initiated participant enrollment and will help to extend the knowledge of a range of vaccines, including Novavax' COVID-19 vaccine, as possible boosters following primary immunization. The Phase 1/2 trial is to assess homologous and heterologous boosting regimens in approximately 1,130 healthy individuals aged 18 years or older received a primary series of a COVID-19 vaccine of whom 180 will receive NVX-CoV2373 as a heterologous booster. Participants will be given a third dose (> 12 weeks later) of either NVX-CoV2373 or one of the three COVID-19 vaccines and followed for 12 months. The Phase 3 trial, which is an observer-blinded, has started enrolling approximately 1,000 participants aged 18 years or older at two centers in Abu Dhabi. The trial aims to evaluate the safety and immunogenicity of a single booster dose of Novavax COVID-19 vaccine in adults previously vaccinated with Sinopharm's COVID-19. Participants will be followed for six months after receipt of the booster. Clinical trial registration #: (NCT04889209 & NCT05249816)
- On 25<sup>th</sup> March 2022, [Icosavax announced topline interim results from its ongoing Phase 1/2 clinical trial of IVX-411, a VLP vaccine candidate displaying the SARS-CoV-2 receptor-binding domain \(RBD\)](#). The ongoing Phase 1/2 clinical trial (IVX-411-01) is a randomised, observer-blinded, placebo-controlled study to evaluate the safety and immunogenicity of IVX-411 in SARS-CoV-2 naïve (N=84) and previously vaccinated (N=84) adults 18 to 69 years of age. Naïve subjects received two doses, given 28 days apart, of IVX-411 at 5, 25 or 125 ug dosage levels or placebo, with or without adjuvant. Previously vaccinated subjects were boosted with a single dose of IVX-411 at 5, 25 or 125 ug or placebo, with or without adjuvant, at 3-6 months following completion of primary licensed vaccine regimen (mRNA or adenoviral). A supplemental analysis was also conducted to assess whether sera from subjects immunized with IVX-411 neutralise the SARS-CoV-2 Omicron variant. IVX-411 was

generally safe and well-tolerated. In the naïve setting, a clear adjuvant effect on immunogenicity and a dose response were observed at day 49 (or three weeks following the second dose), responses were up to 154 IU/mL across dosage groups in the live virus neutralisation assay (HCS: 281 IU/mL), and up to 592 BAU/mL across groups in the spike IgG assay (HCS: 361 BAU/mL). In previously vaccinated subjects, pre- versus post-boost fold increases of up to 5x (599 IU/mL) for wild type virus were observed at day 28 post boost. For the Omicron variant, neutralising antibody titers were up to 8-fold lower than observed for wild type virus in the same assay.

- On 23<sup>rd</sup> March 2022, [Moderna announced positive interim data from the Phase 2/3 KidCOVE study of the Moderna COVID-19 vaccine \(mRNA-1273\) in children 6 months to under 2 years and 2 years to under 6 years of age.](#) KidCOVE is a randomised, observer-blind, placebo-controlled study to evaluate the safety, tolerability, and immunogenicity of two doses of mRNA-1273 given to healthy children 28 days apart. Approximately 11,700 pediatric participants in the U.S. and Canada were enrolled into the trial in 3 age groups (6 to <12 years, 2 to <6 years, and 6 months to <2 years). Interim analysis showed a robust neutralising antibody response in all age groups after a 25 µg two-dose primary series of mRNA-1273 along with a favorable safety profile. Two 25 µg doses of mRNA-1273 vaccine in participants 6 months to <6 years met the primary endpoint with robust neutralising antibody titers similar to adults. mRNA-1273 was generally well tolerated in this age group. Although not a primary endpoint, the vaccine efficacy of mRNA-1273 against the COVID 19 infection during the Omicron wave was consistent with the lower two-dose effectiveness against Omicron seen in adults. Clinical trial registration #: (NCT04796896).
- On 21<sup>st</sup> March 2022, [Mount Sinai Icahn School of Medicine COVID 19 Clinical Trials Unit announced the launch of a Phase 1, open-label, placebo-controlled study to evaluate the safety and immunogenicity of an egg-based COVID-19 vaccine in healthy, vaccinated adults who have never been infected with COVID-19.](#) The egg-based vaccine called NDV-HXP-S contains a recombinant Newcastle disease virus that expresses the spike protein of SARS-CoV-2. It does not contain any adjuvants or preservatives and may have the potential to provide additional immunity against COVID-19. Study participants will receive one of two dose levels of the NDV-HXP-S vaccine as an intranasal, intramuscular, or combined intranasal/intramuscular administration, or placebo. The study is currently being studied in clinical trials in Mexico, Thailand, Brazil, and Vietnam. Clinical trial registration #: (NCT05181709).
- On 17<sup>th</sup> March 2022, [Moderna announced that it has submitted a request to the U.S. Food and Drug Administration \(FDA\) for an amendment to the emergency use authorization \(EUA\) to allow for a fourth dose of the mRNA-1273 COVID-19 vaccine in adults 18 years of age and older who have received an initial booster of any of the authorized or approved COVID-19 vaccines.](#) The request to include adults over 18 years of age provides flexibility for the U.S. Centers for Disease Control and Prevention (CDC) and healthcare providers to determine the appropriate use of an additional booster dose of mRNA-1273, including for those at higher risk of COVID-19 due to age or comorbidities. This submission is based in part on recently published data generated in the United States and Israel following the emergence of Omicron.
- On 17<sup>th</sup> March 2022, [Moderna announced that Health Canada has approved the use of Moderna's mRNA COVID-19 vaccine, SPIKEVAX, in a two-dose series of 50 µg per dose for active immunization to prevent COVID-19 in children aged 6 to 11 years.](#) The approval was based on data analysed from a randomised, observer-blind, placebo-controlled Phase 2/3 "KidCOVE" study to evaluate the safety, tolerability, reactogenicity, and effectiveness of SPIKEVAX (mRNA-1273) given to healthy children 28 days apart. Data from over 4,000 children demonstrated that vaccination of children aged 6 to 11 years with a 50 µg mRNA-1273 primary series is associated with non-inferior anti-SARS-CoV-2 neutralising antibody responses when compared to that in individuals 18 to 25 years old from the Phase 3 COVE study. Positive direct efficacy of two 50 µg doses of mRNA-1273 was also demonstrated, and vaccination was generally well tolerated. Clinical trial registration #: (NCT04796896).
- On 15<sup>th</sup> March 2022, [Pfizer announced submission of an application to the U.S. Food and Drug Administration \(FDA\) for Emergency Use Authorization \(EUA\) of an additional booster dose for adults 65 years of age and older who have received an initial booster of any of the authorized or approved COVID-19 vaccines.](#) The submission is based on two real-world data sets from Israel analyzed at a

time when the Omicron variant was widely circulating. The rates of confirmed infections were 2 times lower and rates of severe illness were 4 times lower among individuals who received an additional booster dose of Pfizer-BioNTech COVID-19 Vaccine compared to individuals who received only an initial booster.

- On 14<sup>th</sup> March 2022, [GeoVax announced the engagement of CATO SMS to manage GeoVax's two ongoing Phase 2 clinical trials of its vaccine candidate, GEO-CM04S1, against SARS-CoV-2](#). GEO-CM04S1 is a synthetic, non-replicating modified vaccinia Ankara (MVA) vaccine vector, developed as a double recombinant vectored vaccine to stimulate potent humoral and cellular immune responses against both the spike (S) and nucleocapsid (N) proteins of the SARS-CoV-2 virus. Upon immunization, the vaccine vector infects cells at the local injection site, leading to the expression of the SARS-CoV-2 antigens that are visible to the immune system. GEO-CM04S1 can likely provide additional recognition elements to the immune system over a homologous boost from mRNA vaccines alone, such as those developed by Moderna or Pfizer/BioNTech, which are directed only toward the S protein. The GEO-CM04S1 vaccine's MVA strongly induce T cell responses even in a background of immunosuppression. Because GEO-CM04S1 targets both S and N antigens, the vaccine may offer greater protection and durability against the significant sequence variation observed with the S antigen among variants of concern such as Omicron. Clinical trial registration #: (NCT04977024 & NCT04639466).

#### Therapeutics trials:

- On 16<sup>th</sup> March 2022, [Shanghai Junshi Biosciences Biosciences announced the first patient was dosed in the Phase 3 trial of VV116 for the treatment of moderate to severe COVID-19](#). The study is an international multicenter, randomised, double-blind, controlled Phase 3 study to evaluate the efficacy and safety of VV116 against standard therapy in subjects with moderate to severe COVID-19. The primary endpoint is the percentage of patients who progress to critical/severe COVID-19 patients or all-cause mortality within 29 days. VV116 is an oral nucleoside analog anti-SARS-CoV-2 investigational drug jointly developed by Junshi Biosciences and Vigonvita Life Sciences. Clinical trial registration #: (NCT05242042).

#### Immunotherapies trials:

- On 28<sup>th</sup> March 2022, [Capricor announced the Phase 2, INSPIRE study evaluating a single-dose intravenous infusion of CAP-1002 as a potential treatment option for hospitalised patients with advanced symptoms of COVID-19 met the study's primary safety objective](#). CAP-1002 consists of allogeneic cardiosphere-derived cells, or CDCs, a type of progenitor cell that has been shown in pre-clinical and clinical studies to exert potent immunomodulatory activity and is being investigated for the potential to modify the immune system's activity to encourage cellular regeneration. All efficacy endpoints were exploratory as the study was not powered to detect treatment differences. In the study of 63 randomised patients, 31% were admitted to the ICU prior to initiation of treatment. The WHO ordinal scale indicated severe disease in 82% of patients (range: 0-8, median 5). The results showed that CAP-1002 was safe, well tolerated and consistent with the historically observed safety profile of the therapy. Overall mortality in the study was 20%, with 6 deaths in the placebo group and 5 deaths in the CAP-1002 group (n=11; p=NS). Clinical trial registration #: (NCT04338347)
- On 28<sup>th</sup> March 2022, [AstraZeneca reported Evusheld \(tixagevimab co-packaged with cilgavimab\), a long-acting antibody combination, has been granted marketing authorisation in the European Union \(EU\) for the pre-exposure prophylaxis \(prevention\) of COVID-19 in a broad population of adults and adolescents aged 12 years and older weighing at least 40 kg](#). The approval based on Phase III PROVENT trial showing a significant 77% risk reduction in developing symptomatic COVID-19, with protection lasting at least six months. The Phase 3 trial is a randomised, double-blind, placebo-controlled, multi-centre assessing the safety and efficacy of a single 300mg dose of AZD7442 compared to placebo for the prevention of COVID-19. The trial was conducted in 87 sites in the US, UK, Spain, France and Belgium. 5,197 participants were randomised in a 2:1 ratio to receive a single intramuscular (IM) dose of either 300mg of AZD7442 (n = 3460) or saline placebo (n = 1,737), administered in two separate, sequential IM injections. The primary efficacy endpoint was the first case

of any SARS-CoV-2 RT-PCR positive symptomatic illness occurring post dose prior to day 183. Clinical trial registration #: (NCT04625725).

- On 25<sup>th</sup> March 2022, [GlaxoSmithKline and Vir announced the US Food and Drug Administration \(FDA\) has amended the Emergency Use Authorization \(EUA\) Fact Sheet for sotrovimab, an investigational monoclonal antibody](#). Sotrovimab is an investigational SARS-CoV-2 neutralising monoclonal antibody. The antibody binds to an epitope on SARS-CoV-2 shared with SARS-CoV-1 indicating that the epitope is highly conserved, decreasing the likelihood for the development of resistance. Based on the totality of available evidence, including new live virus data generated by Vir, the FDA determined that the sotrovimab 500 mg dose will likely not be effective against the Omicron BA.2 variant.
- On 24<sup>th</sup> March 2022, [AstraZeneca reported Evusheld \(tixagevimab co-packaged with cilgavimab\), a long-acting antibody combination, has been recommended for marketing authorisation in the European Union \(EU\) for pre-exposure prophylaxis \(prevention\) of COVID-19 in a broad population of adults and adolescents aged 12 years and older weighing at least 40 kg](#). The recommendation is based on Phase III PROVENT trial showing a significant 77% risk reduction in developing symptomatic COVID-19, with protection lasting at least six months. The Phase 3 trial is a randomised, double-blind, placebo-controlled, multi-centre assessing the safety and efficacy of a single 300mg dose of AZD7442 compared to placebo for the prevention of COVID-19. The trial was conducted in 87 sites in the US, UK, Spain, France and Belgium, and included 5,197 participants randomized in a 2:1 ratio to receive a single intramuscular (IM) dose of either 300mg of AZD7442 (n = 3460) or saline placebo (n = 1,737), administered in two separate, sequential IM injections. The primary efficacy endpoint was the first case of any SARS-CoV-2 RT-PCR positive symptomatic illness occurring post dose prior to day 183. Clinical trial registration #: (NCT04625725).
- On 17<sup>th</sup> March 2022, [AstraZeneca reported that the Medicines and Healthcare products Regulatory Agency \(MHRA\) of UK has licensed Evusheld \(tixagevimab co-packaged with cilgavimab\) the first antibody combination for pre-exposure prophylaxis \(PrEP\) against COVID-19](#). Evusheld is used by unexposed adults and those who are unlikely to mount an adequate response to COVID-19 vaccination including persons for whom COVID 19 vaccine is contraindicated. Based on the primary analysis of 5,172 participants (AZD7442 n = 3,441 and saline placebo n = 1,731), the antibody combination demonstrated a 77% relative risk reduction (RRR) in incidence of symptomatic COVID-19 and 0.8% Absolute Risk Reduction (ARR) compared to placebo, with median follow-up time post-administration of 83 days. After a median 6.5-month follow-up, Evusheld demonstrated a 83% RRR in the incidence of symptomatic COVID-19 and 1.5% ARR compared to placebo. No hospitalisation or deaths were seen in the treatment arm. Clinical trial registration #: (NCT04625725).

**For further detailed information for each country, refer to the full table [here](#)**

### Contributors

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