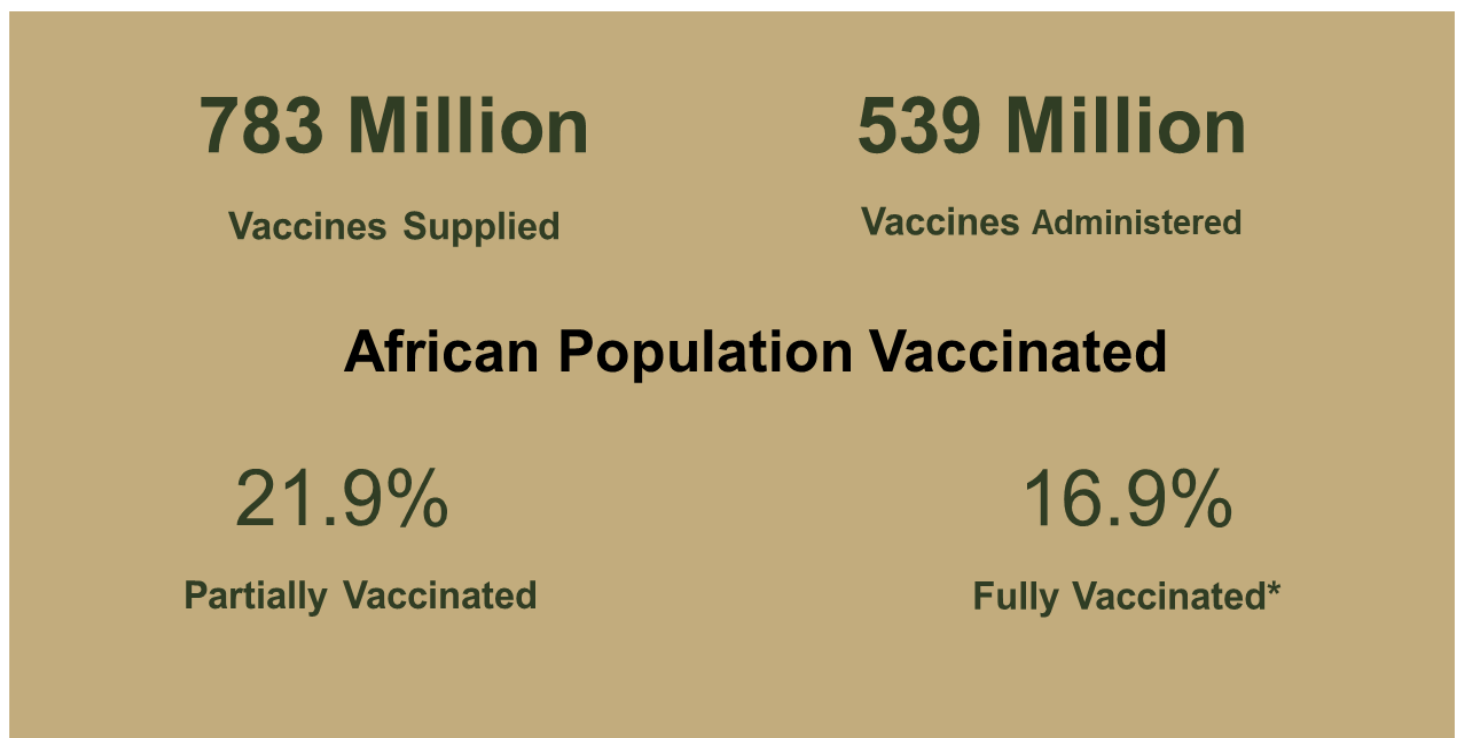


# COVID-19 Scientific and Public Health Policy Update<sup>1</sup> (27 April 2022)

*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 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 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 27<sup>th</sup> April, 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 27 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 27<sup>th</sup> April, 2022

## B. New guidelines and resources

Since 12<sup>th</sup> April 2022,

- Africa CDC<sup>2</sup> has published new guidance and resources on:
  - [Report of the High-Level Ministerial Meeting | Partnerships to Accelerate COVID-19 Vaccination in Africa](#)
  - [Outbreak Brief 118: Coronavirus Disease 2019 \(COVID-19\) Pandemic](#)
  - [The Regional Training And Certification Program For Biosafety And Biosecurity Professionals](#)
  - [Policy Brief for the Legal Framework on Infection Prevention and Control](#)

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

- U.S. CDC<sup>3</sup> has published new guidance and resources on:
  - [CDC Strategy for Global Response to COVID-19 \(2020-2023\)](#)
  - [SARS-CoV-2 Variant Classifications and Definitions](#)
  - [COVID-19 Travel Recommendations by Country](#)
- WHO<sup>4</sup> has published new guidance and resources on:
  - [Infection prevention and control in the context of coronavirus disease \(COVID-19\): a living guideline, 25 April 2022: updated chapter: mask use, part 1: health care settings](#)
  - [WASH FIT: A practical guide for improving quality of care through water, sanitation and hygiene in health care facilities. Second edition](#)
  - [Environmental surveillance for SARS-COV-2 to complement public health surveillance – Interim Guidance](#)
  - [Consolidated report of country success stories in mitigating the impact of the COVID-19 pandemic on TB services](#)
  - [COVID-19 Vaccine Introduction and deployment Costing tool \(CVIC tool\)](#)
  - [Therapeutics and COVID-19: living guideline](#)
  - [5th virtual WHO infodemic management conference meeting report: steps towards measuring the burden of infodemics](#)
- U.S. FDA<sup>5</sup> has issued press releases on:
  - [On 14 April, FDA Authorised First COVID-19 Diagnostic Test Using Breath Samples](#)
  - [On 25 April, FDA Approved First COVID-19 Treatment for Young Children](#)
  - [As of 27 April, 431 tests and sample collection devices are authorised by the FDA under emergency use authorisations](#)
- ECDC<sup>6</sup> has issued new resources on:
  - [A scoping review of point-of-care testing devices for infectious disease surveillance, prevention and control](#)
  - [Overview of the implementation of COVID-19 vaccination strategies and deployment plans in the EU/EEA](#)
- UKHSA<sup>7</sup> has issued new guidance and press releases on:
  - [Living safely with respiratory infections, including COVID-19](#)
  - [COVID-19: infection prevention and control \(IPC\)](#)

## C. Scientific updates

### Basic Science

- This [cohort study](#) in Italy assessed T-cell reactivity to the Omicron variant in individuals with established (natural and/or vaccine-induced) immunity to SARS-CoV-2. The study involved 61 health care worker and scientist volunteers. The median (range) frequency of CD4<sup>+</sup> T cells reactive to peptides covering the mutated regions in the Omicron variant was 0.039% (0%-2.356%), a decrease of 64% compared with the frequency of CD4<sup>+</sup> cells specific for the same regions of the ancestral strain (0.109% [0%-2.376%]). Within CD8<sup>+</sup> T cells, a median (range) of 0.02% (0%-0.689%) of cells recognized the mutated spike regions, while 0.039% (0%-3.57%) of cells were reactive to the equivalent unmutated regions, a reduction of 49%. However, overall reactivity to the peptide library of the full-length protein was largely maintained (estimated 87%). No significant differences in loss of immune recognition were identified between groups of participants with different vaccination or infection histories. These findings suggest

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

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

<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

that cellular immunity to the Omicron variant, together with protection from severe disease, will not be compromised despite mutations to the SARS-CoV-2 spike protein.

- This [cohort study](#) characterized the humoral and cellular immune responses in vaccinated individuals from Provincetown, Massachusetts who did or did not develop a breakthrough case of SARS-CoV-2. Vaccinated individuals who tested positive for SARS-CoV-2 ( $n = 16$ ) demonstrated substantially higher serum antibody responses than vaccinated individuals who tested negative for SARS-CoV-2 ( $n = 23$ ), including 32-fold higher binding antibody titers and 31-fold higher neutralising antibody titers against the SARS-CoV-2 Delta variant. Vaccinated individuals who tested positive also showed higher mucosal antibody responses in nasal secretions and higher spike protein-specific CD8<sup>+</sup> T cell responses in peripheral blood than did vaccinated individuals who tested negative. These data demonstrate that fully vaccinated individuals developed robust anamnestic antibody and T cell responses after infection with the SARS-CoV-2 delta variant. Moreover, these findings suggest that population immunity will likely increase over time by a combination of widespread vaccination and breakthrough infections.
- This [study](#) in China analysed sequences from a large number of Omicron subvariants. Diverse recombination events between two Omicron subvariants (BA.1 and BA.2) and several SARS-CoV-2 variants of concern (VOCs) and variants of interest (VOIs) were identified. These recombination events include “Deltacron”-like variants, suggesting that co-infection and subsequent genome recombination play important roles in the on-going evolution of SARS-CoV-2. Monitoring the evolving SARS-CoV-2 genomes, especially for recombination is critically important for recognition of abrupt changes to viral attributes, such as to the virus’ epitopes, which may call for vaccine modifications.

### Vaccines

- This [secondary analysis](#) of the phase 3 ENSEMBLE trial (NCT04505722) assessed the impact of preexisting humoral immunity to adenovirus type 26 (Ad26) on the immunogenicity of Ad26.COV2.S-elicited SARS-CoV-2-specific antibody levels in 380 participants in Brazil, South Africa, and the United States. Among the vaccinated participants in Brazil and South Africa, 31% (27/86) and 66% (53/80), respectively, had prevaccination serum-neutralising activity against Ad26. Vaccinated participants in the United States (2%, 1/48) had little preexisting immunity.). Geometric mean concentrations against the spike protein increased to 402 (95% confidence interval [CI] 321–505), 388 (95% CI: 297–506), and 412 (95% CI: 306–554) in the Brazil, South Africa, and United States groups, respectively. These findings indicate that baseline immunity to Ad26 has no clear impact on vaccine-induced immune responses.
- This [study](#) in Israel assessed the relative effectiveness of a fourth dose of the BNT162b2 vaccine in preventing COVID-19-related outcomes among  $\geq 60$ -year-olds. The relative effectiveness of the fourth vaccine dose was compared with that of a third dose given at least 4 months earlier. The analysis included 182,122 matched pairs (individually matched on multiple sociodemographic and clinical variables). Relative vaccine effectiveness in days 7 to 30 after the fourth dose was estimated to be 45% (95% CI: 44 to 47) against PCR-confirmed SARS-CoV-2 infection, 55% (95% CI: 53 to 58) against symptomatic COVID-19, 68% (95% CI: 59 to 74) against COVID-19-related hospitalisation, 62% (95% CI: 50 to 74) against severe COVID-19, and 74% (95% CI: 50 to 90) against COVID-19-related death. The corresponding estimates in days 14 to 30 after the fourth dose were 52% (95% CI, 49 to 54), 61% (95% CI: 58 to 64), 72% (95% CI: 63 to 79), 64% (95% CI: 48 to 77), and 76% (95% CI: 48 to 91). These findings indicate that a fourth dose of the BNT162b2 vaccine was effective in reducing the short-term risk of COVID-19-related outcomes among persons who had received a third dose at least 4 months earlier.
- Six national [matched, test-negative case-control studies](#) in Qatar assessed the effectiveness of BNT162b2 vaccine, mRNA-1273 vaccine, natural immunity due to prior infection with pre-Omicron variants, and hybrid immunity from prior infection and vaccination. The five different forms of immunity were investigated against SARS-CoV-2 Omicron symptomatic BA.1 infection, symptomatic BA.2 infection, BA.1 hospitalisation and death, and BA.2 hospitalisation and death. There were no discernable differences in the effects of prior infection, vaccination, and hybrid immunity against BA.1 versus BA.2. Effectiveness of hybrid immunity resulting from prior infection and recent booster vaccination (77.3% [95% CI: 72.4-81.4%]) conferred the strongest protection against either subvariant.

Vaccination enhanced protection of those with a prior infection. All five forms of immunity showed strong effectiveness >70% against any severe, critical, and fatal COVID-19. [*not peer reviewed*]

- This [cohort study](#) in 4 Nordic countries (Denmark, Finland, Norway, and Sweden) assessed the risks of myocarditis and pericarditis following SARS-CoV-2 vaccination. The study involved 23.1 million residents aged 12 years or older who were followed from 27 December 2020 until incident myocarditis or pericarditis, censoring (positive test result for SARS-CoV-2 infection, receiving Ad26.COV2.S vaccine, receiving a third dose of any SARS-CoV-2 vaccine, emigration or death), or the completion of the study (5 October 2021). At the end of the study, 81% of the participants were vaccinated. A total of 1,077 incident myocarditis events and 1,149 incident pericarditis events were identified. Within 28 days post vaccination, for both males and females who received a homologous schedule, the second dose was associated with higher risk of myocarditis, with adjusted IRRs of 1.75 (95% CI, 1.43-2.14) for BNT162b2 and 6.57 (95% CI, 4.64-9.28) for mRNA-1273. Among males 16 to 24 years of age, adjusted IRRs were 5.31 (95% CI, 3.68-7.68) for a second dose of BNT162b2 and 13.83 (95% CI, 8.08-23.68) for a second dose of mRNA-1273, and numbers of excess events were 5.55 (95% CI, 3.70-7.39) events per 100,000 vaccinees after the second dose of BNT162b2 and 18.39 (9.05-27.72) events per 100,000 vaccinees after the second dose of mRNA-1273. Estimates for pericarditis were similar. The risk of myocarditis associated with SARS-CoV-2 vaccine must be balanced against the expected benefits in prevention of severe COVID-19 disease.

#### Diagnosics

- This [study](#) in Australia described the designing, implementation, and performance of a mobile laboratory (LabVan) for rapid SARS-CoV-2 diagnostics, benchmarked against a central reference laboratory. The LabVan is a BSL2 compliant laboratory, complete with a class II biological safety cabinet, built within a Mercedes-Benz Sprinter Panel Van. Swabs were collected by on-site collection teams, registered using mobile internet-enabled tablets and tested using the Xpert® Xpress SARS-CoV-2 assay. A pilot trial of the LabVan identified a median turnaround time (TAT) from collection to reporting of 1:19 h:mm (IQR 0:18, Range 1:03–18:32) compared to 9:40 h:mm (IQR 8:46, Range 6:51–19:30) for standard processing within the central laboratory. During deployment in nine rural and urban COVID-19 outbreaks, the median TAT was 2:18 h:mm (IQR 1:18, Range 0:50–16:52) compared to 19:08 h:mm (IQR 5:49, Range 1:36–58:52) for samples submitted to the central laboratory. No quality control issues were identified in the LabVan.

#### Care and Treatment

- This [systematic review and meta-analysis](#) of 20 studies assessed whether drug interaction checkers could identify adverse events associated with drug-drug interactions (DDIs) in patients with COVID-19. The 20 studies enrolled a total of 1,297 patients. The DDIs identified in the reviewed articles involved 46 different drugs. The drug interaction checkers used in this study were Drugs.com, COVID-19 Drug Interactions, LexiComp, Medscape, and WebMD. In total, 575 DDIs for 58 drug pairs (305 associated with at least 1 adverse drug reaction) were reported. The drugs most commonly involved in DDIs were lopinavir and ritonavir. The studies reported 115 DDI-related adverse events: 15 (26%) were identifiable by all tools analysed, 29 (50%) were identifiable by at least 1 of them, and 14 (24%) remained nonidentifiable. These findings suggest that the use of drug interaction checkers can help identify several DDI-associated adverse drug reactions, including severe and life-threatening events. Interactions between the drugs used to treat COVID-19 and those already used by the patients for pre-existing conditions should be evaluated.
- This [non-randomised controlled trial](#) in the United States assessed whether awake prone positioning is associated with improved outcomes among patients with COVID-19-related hypoxemia who have not received mechanical ventilation. The study involved 501 patients who were assigned in a 1:1 ratio to receive either the practitioner-recommended awake prone positioning intervention (intervention group) or usual care (usual care group). On study day 5, the bayesian posterior probability of the intervention group having worse outcomes than the usual care group on the modified World Health Organization ordinal outcome scale was 0.998 (posterior median adjusted odds ratio [aOR], 1.63; 95% credibility interval [CrI], 1.16-2.31). On study days 14 and 28, the posterior probabilities of harm were 0.874 (aOR, 1.29; 95% CrI, 0.84-1.99) and 0.673 (aOR, 1.12; 95% CrI, 0.67-1.86), respectively.

Exploratory outcomes (progression to mechanical ventilation, length of stay, and 28-day mortality) did not differ between groups.

- This [randomised, double-blind, placebo-controlled, phase 2 clinical trial](#) in the United States assessed whether famotidine improved inflammation and symptomatic recovery in outpatients with mild to moderate COVID-19. The study involved 55 symptomatic unvaccinated adults between January 2021 and April 2021 from two centres. Patients self-administered 80 mg famotidine (n=28) or placebo (n=27) orally three times a day for 14 consecutive days. Time to symptom resolution by study day 28 (primary endpoint) was not statistically improved (p=0.4) between patients in the famotidine and placebo arm. Rate of symptom resolution (secondary endpoint) was improved for patients taking famotidine (p<0.0001). Estimated 50% reduction of overall baseline symptom scores were achieved at 8.2 days (95% CI: 7 to 9.8 days) for famotidine and 11.4 days (95% CI: 10.3 to 12.6 days) for placebo treated patients. Differences were independent of patient sex, race or ethnicity. Five self-limiting adverse events occurred (famotidine, n=2 (40%); placebo, n=3 (60%)). On day 7, fewer patients on famotidine had detectable interferon alpha plasma levels (p=0.04). Plasma immunoglobulin type G levels to SARS-CoV-2 nucleocapsid core protein were similar between both arms. Famotidine was safe and well tolerated in outpatients with mild to moderate COVID-19. Famotidine led to earlier resolution of symptoms and inflammation without reducing anti-SARS-CoV-2 immunity. Additional randomised trials are required.

### Epidemiology

- This [prospective study](#) assessed the main viral etiologies associated with encephalitis and described the clinical presentation of encephalitis patients in Senegal. The study enrolled 122 patients across two neurology wards of two hospitals located in Dakar and Pikine from January to December 2021. The main neurological symptoms were impaired consciousness (52%), motor deficit (37%), meningeal syndrome (37%), behavioral changes (30%), cranial nerve damage (30%), and seizures (26%). The main extra-neurological symptoms included respiratory disorders (19%), arthralgia/myalgia (19%), and anosmia (11%). Cerebrospinal fluids, blood, and nasopharyngeal swabs were taken and tested for 27 viruses. Viral etiology was confirmed or probable in 27 patients (22.1%), with SARS-CoV-2 (n = 8), HSV-1 (n = 7), HHV-7 (n = 5), and EBV (n = 4) being the most detected viruses. Age groups 40–49 was more likely to be positive for at least one virus with an odds ratio of 7.7 [95% CI: 1.8–41.7]. The mortality was high among infected patients, with 11 (41%) deaths notified during hospitalisation. Interestingly, SARS-CoV-2 was the most prevalent virus in hospitalised patients presenting with encephalitis. These findings reveal the crucial need to establish a country-wide surveillance of encephalitis to estimate the burden of the disease and implement strategies to improve care and reduce mortality.
- This [study](#) compared epidemiologic characteristics of hospitalised patients (HP) and non-hospitalised patients (NHP) with COVID-19 during the two waves of COVID-19 in Uganda. The study involved a total of 800 patients, 400 HP were recruited from the two highest-volume referral hospitals in Uganda. The second wave of SARS-CoV-2 infections in Uganda (April–June 2021) was caused primarily by the Delta variant, while the first wave (November–December 2020) was caused by a mixture of non-Delta variants. Infections in Waves 1 and 2 in Uganda differed across several indicators. HP were more likely to be male in Wave 1 than in Wave 2 (73% vs 54%; p<0.01). NHP were younger in Wave 2 than in Wave 1, but this difference was not significant (mean age 29 vs 36 years; p=0.13). Increasing age was strongly associated with hospitalisation during Wave 2 (mean age 48 vs 29 years; p<0.01), but was only marginally associated with hospitalisation in Wave 1 (mean age 48 vs 43 years; p=0.31). A higher proportion of HP had severe disease and died in Wave 2 than in Wave 1 (65% vs 31%; p<0.01). The findings emphasize the need to study and understand the epidemiologic characteristics of each SARS-CoV-2 variant independently to ensure that messaging and preparedness are tailored appropriately in each wave.
- This [cohort study](#) in Italy assessed the prevalence of SARS-CoV-2–related conjunctival manifestations and conjunctival swab (CS) positivity on hospital admission (T1) and 3 days thereafter (T2) in patients not receiving anti-inflammatory treatment. The study involved 142 patients across 3 tertiary hospitals. Eighteen patients (12.7%) had a positive CS result; 64 (45.1%) had at least 1 clinical finding (eg,

conjunctival redness (CR), most commonly grade 2). The CR grade was significantly higher in eyes with CS positivity ( $p < .001$ ). At T2, 12 patients (8.5%) had a positive CS result. There were 5 additional patients in the non-artificial tears group ( $p = .10$ ) and 14 fewer patients in the artificial tears group ( $p = .001$ ). Redness worsened among non-treated eyes ( $p = .001$ ), whereas both CR and other conjunctival signs and symptoms (OCSSs) improved among artificial tears-treated eyes (both  $p < .001$ ). Compared with preservative free-artificial tears, these results suggest that non-preservative free-artificial tears were 1.13 times more effective at improving CR and were the only formulation in this study able to reduce OCSS and CS positivity.

- This [prospective study](#) in the U.S assessed infections, illness severity, vaccinations, and early neonatal infections among obstetric patients during the pre-Delta, Delta, and Omicron epochs. There were 2,641 SARS-CoV-2 infections diagnosed in pregnancy, 1298 (median, 17 cases per week) during the pre-Delta epoch, 431 (median, 14 cases per week) during Delta, and 912 (median, 138 cases per week) during Omicron. Compared with the pre-Delta epoch, periods of Delta and Omicron predominance were associated with increased infections (incidence rate ratios, 3.07 [95% CI, 2.46-3.82] and 10.09 [95% CI, 7.42-13.69], respectively). Delta predominance was associated with increased odds (OR, 2.93 [95% CI, 1.18-7.69]) and Omicron associated with decreased odds of severe or critical illness in pregnancy compared with pre-Delta infections after adjusting for vaccination (OR, 0.20 [95% CI, 0.05-0.83]). Of 1,919 infants delivered during the study period, 1015 were tested and 32 (3.1%) were positive for SARS-CoV-2 (13 during pre-Delta, 8 during Delta, and 11 during Omicron epochs); none had significant illness. No difference in early neonatal positivity in the pre-Delta, Delta, or Omicron epochs was detected ( $p = .39$ ).
- This [cohort study](#) in the UK assessed recovery 1 year after hospital discharge for COVID-19, identified factors associated with patient-perceived recovery, and described potential therapeutic targets. The study involved 2,320 participants discharged from hospital between March 2020 and April 2021. The proportion of patients reporting full recovery was unchanged between 5 months (25.5%, 501/1965) and 1 year (28.9%, 232/ 804). Factors associated with being less likely to report full recovery at 1 year were female sex (odds ratio [OR] = 0.68 [95% CI 0.46–0.99]), obesity (OR = 0.50 [0.34–0.74]) and invasive mechanical ventilation (OR = 0.42 [0.23–0.76]). Several inflammatory mediators were increased in individuals with the most severe physical, mental health, and cognitive impairments compared with individuals with milder ongoing impairments. Their results support the use of a precision-medicine approach with potential treatable traits of systemic inflammation and obesity.

#### Infection prevention & control

- This [ongoing, multicenter, double-blind, randomised trial](#) assessed the safety and efficacy of a single dose of AZD7442 (tixagevimab and cilgavimab) for the prevention of symptomatic and severe COVID-19 in adults. The trial is being conducted at 87 sites in Belgium, France, Spain, the United Kingdom, and the United States. The study has enrolled 5,197 participants who underwent randomisation and received one dose of AZD7442 or placebo (3,460 in the AZD7442 group and 1,737 in the placebo group). In total, 35.3% (1,221/3,461) of participants in the AZD7442 group and 34.2% (593/1,736 participants in the placebo group reported having at least one adverse event, most of which were mild or moderate in severity. Symptomatic COVID-19 occurred in 0.2% (8/3,441) of participants in the AZD7442 group and in 1.0% (17/1,731) in the placebo group (relative risk reduction, 76.7%; 95% confidence interval [CI]: 46.0 to 90.0); extended follow-up at a median of 6 months showed a relative risk reduction of 82.8% (95% CI: 65.8 to 91.4). Five cases of severe or critical COVID-19 and two COVID-19–related deaths occurred, all in the placebo group. Findings support the use of a single dose of AZD7442 for the prevention of symptomatic and severe COVID-19 disease.
- This [decision analytical model study](#) in the United States assessed the health outcomes and net cost of implementing postexposure prophylaxis (PEP) with monoclonal antibodies (mAbs) against household exposure to COVID-19. For a month with transmission intensity similar to that of May 2021, a monoclonal antibody PEP program reaching 50% of exposed, unvaccinated household members aged 50 years and older was estimated to avert 528 hospitalisations (95% uncertainty interval [UI], 354-724) and 84 deaths (95% UI: 55-116) in a low-transmission scenario. Assuming the same intervention reach, the program was estimated to avert 1,404 hospitalisations (95% UI: 974-1827) and

223 deaths (95% UI, 152-299) in a high-transmission scenario. The program was also estimated to be cost-saving to payers in the high-transmission scenario as a result of averted hospitalisations. These findings suggest that COVID-19 PEP with monoclonal antibodies may be associated with reduced costs and improved population health.

#### Non-pharmaceutical interventions, social distancing

- This [prospective cohort study](#) quantified workplace contact patterns by occupation and over time during the second and third waves of the COVID-19 pandemic in England. The study involved 4,616 participants who submitted electronic contact information from November 2020 to November 2021. Workplace attendance and contact patterns varied across occupations and time. The predicted probability (PP) of intense space sharing during the day was highest for healthcare (PP = 78%, 95% CI: 75–81%) and education workers (PP = 64%, 95% CI: 59%–69%), who also had highest probabilities for having large number of close contacts 36% (95% CI: 32%–40%) and 38% (95% CI: 33%–43% respectively). Education workers also demonstrated relatively low predicted probability (PP = 51%, 95% CI: 44%–57%) of wearing a face covering during close contact. Across all occupational groups, workspace sharing and close contact increased and usage of face coverings decreased during phases of less stringent restrictions. These findings are concerning given ongoing high levels of community transmission and emergence of variants.

## D. Clinical Trials Updates

### Key updates:

#### Vaccine trials:

- On 22 April 2022, [Novavax has initiated administration of the first booster doses of NVX-CoV2373 in the pediatric expansion of the PREVENT-19 pivotal Phase 3 clinical trial](#). The study will evaluate the safety and immunogenicity of a third dose of NVX-CoV2373 among trial participants aged 12 through 17 years. NVX-CoV2373 is a protein-based vaccine engineered from the genetic sequence of the first strain of SARS-CoV-2, the virus that causes COVID-19 disease. The phase 3 trial is a randomised, observer-blinded, placebo-controlled study to evaluate the efficacy, safety, and immunogenicity of SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) in adult participants aged 18 years and above in adult main study and pediatric participants aged 12 through 17 years in pediatric expansion study. All trial participants aged 12 through 17 are eligible to receive a third booster dose of NVX-CoV2373 which is identical to the active vaccine previously administered to the participants in a two-dose regimen (5 micrograms of recombinant spike protein plus 50 micrograms of Matrix-M adjuvant) and may be administered at least five months after receipt of active vaccine. The post-booster objectives include the assessment of the humoral immune response 28 days after the administration of the booster dose and describing COVID-19 disease events. Clinical trial registration #: (NCT04611802).
- On 20 April 2022, [Novavax announced initial results from the Phase 1/2 clinical trial of its COVID-Influenza Combination Vaccine \(CIC\)](#). The CIC combines Novavax' COVID-19 vaccine, NVX-CoV2373, with a quadrivalent influenza vaccine candidate. NVX-CoV2373 is a protein-based vaccine engineered from the genetic sequence of the first strain of SARS-CoV-2, the virus that causes COVID-19 disease. The Phase 1/2 CIC vaccine trial conducted in Australia is evaluating a combination of Novavax' recombinant protein-based NVX-CoV2373 and influenza vaccine candidates and patented saponin-based Matrix-M adjuvant in a single formulation. The trial evaluate the safety, tolerability and immune response to the combination vaccine in 642 healthy adults 50 to 70 years of age. Participants have been either previously infected with the SARS-CoV-2 virus or vaccinated through an authorised vaccine at least eight weeks prior to enrollment. All participants were randomly assigned to cohorts to evaluate multiple formulations and dosed on Day 0 and again at Day 56. The preliminary trial results found that various CIC vaccine formulations induced immune responses in participants comparable to reference stand-alone influenza and stand-alone COVID-19 vaccine formulations (for H1N1, H3N2, B-Victoria HA and SARS-CoV-2 rS antigens). The CIC trial demonstrated that formulating the combination vaccine is feasible, well-tolerated and immunogenic. The safety and tolerability profile of the combination vaccine was consistent with the stand-alone NVX-CoV2373 and quadrivalent nanoparticle



influenza vaccine reference formulations in the trial. The combination vaccine was found to be generally well tolerated. Serious adverse events were rare and none were assessed as being related to the vaccine. Clinical trial registration #: (NCT04961541).

- On 14 April 2022, [Valneva announced that the Medicines and Healthcare products Regulatory Agency \(MHRA\) of the United Kingdom has granted Conditional Marketing Authorisation \(CMA\) for the company's inactivated whole-virus COVID-19 vaccine candidate, VLA2001, for primary immunization in adults 18 to 50 years of age.](#) The MHRA found that VLA2001 meets the required safety, quality and effectiveness standards. VLA2001 is currently the only whole virus, inactivated, adjuvanted vaccine candidate in clinical trials against COVID-19 in Europe. The vaccine is intended for active immunization of at-risk populations to prevent carriage and symptomatic infection with COVID-19 during the pandemic and for routine vaccination including addressing new variants. VLA2001 may also be suited for boosting, as repeat booster vaccinations have been shown to work well with whole virus inactivated vaccines.
- On 14 April 2022, [Pfizer and BioNTech announced positive results from a phase 2/3 clinical trial evaluating the safety, tolerability and immunogenicity of a 10-µg booster \(third\) dose of the Pfizer-BioNTech COVID-19 vaccine in healthy children 5 through 11 years of age.](#) The phase 2/3 is a placebo-controlled, observer-blinded study to evaluate safety, tolerability, and immunogenicity of a SARS-CoV-2 RNA vaccine candidate against COVID-19 in healthy children and young adults. Data from 140 children aged 5 through 11 years received a booster dose approximately 6 months after the second dose of the Pfizer-BioNTech COVID-19 vaccine 10-µg primary series were analyzed. The immunogenicity data among those without evidence of prior SARS-CoV-2 infection showed a 6-fold increase (95% CI: 5.0, 7.6) in SARS-CoV-2 wild-type strain–neutralising geometric mean titers (GMTs) one month after the booster compared to one month after the second dose of the Pfizer-BioNTech COVID-19 vaccine, demonstrating a strong immune response in this age group. A sub analysis of sera collected from 30 participants indicate that serum antibodies induced by a third dose neutralise the SARS-CoV-2 Omicron variant in this age group, as demonstrated by a 36-fold increase in neutralising antibody titers compared to levels seen after two doses of the Pfizer-BioNTech COVID-19 Vaccine. A robust response was observed regardless of prior SARS-CoV-2 infection. These data reinforce the potential benefits of a third vaccine dose in maintaining high levels of protection against the virus in children 5 to 11 years of age. Clinical trial registration #: (NCT04816643).
- On 14 April 2022, [Sinovac announced its inactivated COVID-19 vaccine \(Omicron strain\) has been approved for clinical trial in Hong Kong, China.](#) The trial objectives is to evaluate the inactivated COVID-19 vaccine (Omicron strain) safety and effectiveness. Preclinical research in animals demonstrated the vaccine is safe and effective. The clinical approval in Hong Kong is the first for the SINOVARC Omicron strain inactivated vaccine.

#### Therapeutics trials:

- On 25 April 2022, [Veru has reported positive findings from the Phase 2 clinical trial of oral sabizabulin in individuals with severe Covid-19 who are at increased risk for acute respiratory distress syndrome \(ARDS\).](#) The phase 2 study is a double-blind, randomised, placebo-controlled clinical trial to evaluate oral, once-a-day dosing of sabizabulin versus placebo in approximately 40 hospitalised COVID-19 patients who were at high risk for ARDS. The trial was conducted in five sites across the United States. Subjects received daily oral dosing of sabizabulin or placebo and standard of care for 21 days or until released from hospital. The primary efficacy endpoint was the proportion of patients alive without respiratory failure at Day 29. Respiratory failure was defined as endotracheal intubation and mechanical ventilation, extracorporeal membrane oxygenation, high-flow nasal cannula oxygen delivery, noninvasive positive pressure ventilation, and/or clinical diagnosis of respiratory failure with initiation of none of these measures only when clinical decision making is driven solely by resource limitation. Compared to the placebo group, Sabizabulin treatment resulted in an 82% relative reduction in deaths ( $p=0.04$ ). Further, sabizabulin treatment resulted in a reduction in mean days in the ICU from  $9.6 \pm 12.40$  days in the placebo group to  $2.6 \pm 5.78$  days ( $p = 0.03$ ) in the treatment group, a 73% relative reduction in the mean days in the ICU. Similarly, there was a reduction in mean days on mechanical ventilation from  $5.1 \pm 11.24$  days in the placebo group to  $1.2 \pm 6.06$  days ( $p=0.147$ ), a 78%

relative reduction in days on mechanical ventilation. Sabizabulin was safe and well tolerated with no treatment related adverse events observed on the study. Clinical trial registration #: (NCT04842747).

- On 25 April 2022, [Gilead announced that the U.S. Food and Drug Administration \(FDA\) has approved a supplemental new drug application \(sNDA\) for Veklury \(remdesivir\) for treatment of pediatric patients who are older than 28 days, weighing at least 3 kg, and are either hospitalised with COVID-19 or have mild-to-moderate COVID-19 and are considered high risk for progression to severe COVID-19, including hospitalisation or death.](#) The approval is based on results from the CARAVAN Phase 2/3 single arm, open-label study, which demonstrated that Veklury is generally well-tolerated among pediatric patients hospitalised with COVID-19, with a high proportion of participants showing clinical improvement and recovery. Of the 53 pediatric patients enrolled in the CARAVAN study, no new safety signals were apparent among patients treated with Veklury. Overall, 75% and 85% showed clinical improvement ( $\geq 2$  point increase on the ordinal scale) at Day 10 and last assessment, respectively, while 60% and 83% were discharged by Day 10 and Day 30, respectively. In the study 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, including three participant deaths. The deaths were consistent with patients' underlying medical conditions prior to study entry or with COVID-19 disease during hospitalisation. Clinical trial registration #: (NCT04431453).
- On 24 April 2022, [Shionogi announced new results from two late-breaking presentations of S-217622 an investigational 3CL protease inhibitor that was studied for once-daily oral administration in mainly vaccinated patients \(~85%\), with no risk factors for severe complications, within five days of COVID-19 symptom onset.](#) S-217622 (an investigational therapeutic drug for COVID-19) is a 3CL protease inhibitor that inhibits 3CL protease enzyme which is essential for the replication of SARS-CoV-2 virus. The Phase 2b results from the Phase 2/3 clinical trial of S-217622, completed in Asia showed S-217622 demonstrated rapid clearance of the infectious SARS-CoV-2 virus. On day four of treatment (following the third dose), the proportion of patients with positive viral titer decreased by approximately 90% versus placebo. The treatment shortened infectious virus shedding by 1-2 days versus placebo with a significant reduction in viral RNA on days 2, 4, 6 and 9 versus placebo. The trial demonstrated that S-217622 was generally well-tolerated (only a few patients discontinued treatment due to side effects), and no reports of serious adverse events or deaths occurred. Clinical trial registration #: (NCT05305547).
- On 21 April 2022, [World Health Organization \(WHO\) announced that it strongly recommends the use of Paxlovid \(nirmatrelvir and ritonavir\) for mild and moderate COVID-19 patients at the highest risk of hospital admission.](#) Paxlovid is strongly recommended for patients with non-severe COVID-19 who are at the highest risk of developing severe disease and hospitalisation, such as unvaccinated, older, or immunosuppressed persons. The recommendation is based on new data from two randomised controlled trials involving more than 3,000 patients. Risk of hospitalisation was reduced by 85% among patients receive the treatment compared to those who did not. In a high-risk group, thi means 84 fewer hospitalisations per 1,000 patients. Use for patients at lower risk is not recommended, as the benefits were found to be negligible.
- On 21 April 2022, [NRx Pharmaceuticals announced submission of a new Breakthrough Therapy designation request with the U.S. Food and Drug Administration \(FDA\) focused on a subgroup of patients with Critical COVID-19 that in addition to ZYESAMI \(aviptadil\) or placebo were also treated with remdesivir.](#) The request was supported by the analysis of completed Phase IIb/III study data focused on the approximately 70% of patients that continued to progress to COVID-19 respiratory failure who also received treatment with remdesivir. The analysis showed that for patients, who were already treated with remdesivir and continued to progress, ZYESAMI showed a highly significant four-fold increased odds of survival compared to placebo at 60 days ( $p=.001$ ). Safety data on approximately 750 patients treated with intravenous ZYESAMI for Critical COVID-19 revealed no new adverse drug reactions and an overall safety profile that is congruent with use in ICU/Critical Care settings. Clinical trial registration #: (NCT04311697).
- On 19 April 2022, [Ascletis announces that its oral small molecule drug candidate ASC11, a 3-chymotrypsin like protease \(3CLpro\) inhibitor, demonstrated potential to be effective treatment for COVID-19.](#) The Investigational New Drug (IND) ASC11 is an in-house discovered oral small molecule

drug candidate using molecular docking that compared to Nirmatrelvir, ASC11 formed stronger hydrogen bond interaction with Glutamic acid 166 of 3CLpro, created new hydrogen bonds with other key amino acids of 3CLpro and fitted more tightly in hydrophobic Pocket 4 (P4) of 3CLpro, resulting in much higher antiviral potency (EC90) of ASC11. In antiviral cellular assays with infectious SARS-CoV-2, antiviral potency (EC90) of ASC11 is 31-fold (155/5) of that of Nirmatrelvir; 120-fold (600/5) of that of S-217622; 16-fold (78/5) of that of PBI-0451 and 7-fold (33/5) of that of EDP-235. Importantly, ASC11 activity was retained against different SARS-CoV-2 variants. Together with other preclinical data, including Caco-2 permeability, in vitro metabolism, microsomal stability and animal pharmacokinetic studies, ASC11 demonstrated potential for antiviral treatment of COVID-19.

- On 13 April 2022, [SyneuRx International announced complementation of enrollment for a phase 2 clinical trial aimed at evaluating the efficacy and safety of SNB01 \('Pentarlandir'\), a novel COVID-19 oral antiviral candidate](#). Pentarlandir is a potent protease regulatory enzymes blocker that has ability to block coronavirus replication in multiple, rigorous cellular studies and proved to maintain an excellent safety profile. The phase 2 trial is a randomised, double-blind, placebo-controlled study involving 89 participants suffering from unvaccinated or early-stage breakthrough cases of COVID-19, randomised evenly into high-dose, low-dose, and placebo groups. In preclinical studies, Pentarlandir demonstrated preliminary efficacy and an excellent safety profile against Omicron, Delta, and previously identified variants of concern, in addition to several influenza viruses. Clinical trial registration #: (NCT04911777).

#### Immunotherapies trials:

- On 14 April 2022, [Regeneron announced the U.S. Food and Drug Administration \(FDA\) has extended the review of the Biologics License Application \(BLA\) for REGEN-COV \(casirivimab and imdevimab\) to treat COVID-19 in non-hospitalised patients and as prophylaxis in certain individuals by three months](#). The extension resulted from the submission of additional data from a completed prophylaxis trial on pre-exposure prophylactic use. REGEN-COV (casirivimab and imdevimab) is a cocktail of two monoclonal antibodies designed specifically to block infectivity of SARS-CoV-2, the virus that causes COVID-19. Clinical trial registration #: (NCT04452318).
- On 12 April 2022, [BioCardia announced the U.S. Food and Drug Administration \(FDA\) has approved the Investigational New Drug \(IND\) application for BCDA-04, a proprietary allogeneic mesenchymal cell \(MSC\) population that is Neurokinin-1 receptor positive \(NK1R+\)](#). This allows initiation of First-in-Human Phase 1/2 trial in adult patients recovering from Acute Respiratory Distress Syndrome (ARDS) due to COVID-19. The first part of the clinical trial will evaluate increasing doses of the NK1R+ MSCs and the optimal dose will be taken to Phase 2 in a randomised study in adult patients recovering from ARDS due to COVID-19. The investigational cell therapy is administered intravenously (IV) and cells migrate to the lungs for local therapeutic benefit. The anti-inflammatory nature of these mesenchymal stem cells is expected to have a positive impact in ARDS due to the interaction of the Neurokinin-1 receptors with Substance P, a neuropeptide that has long been known to be a primary mediator of inflammation in the lungs. This will make patients with ARDS due to COVID-19 recover faster and more fully, while avoiding longer term respiratory issues.

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

#### Contributors

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