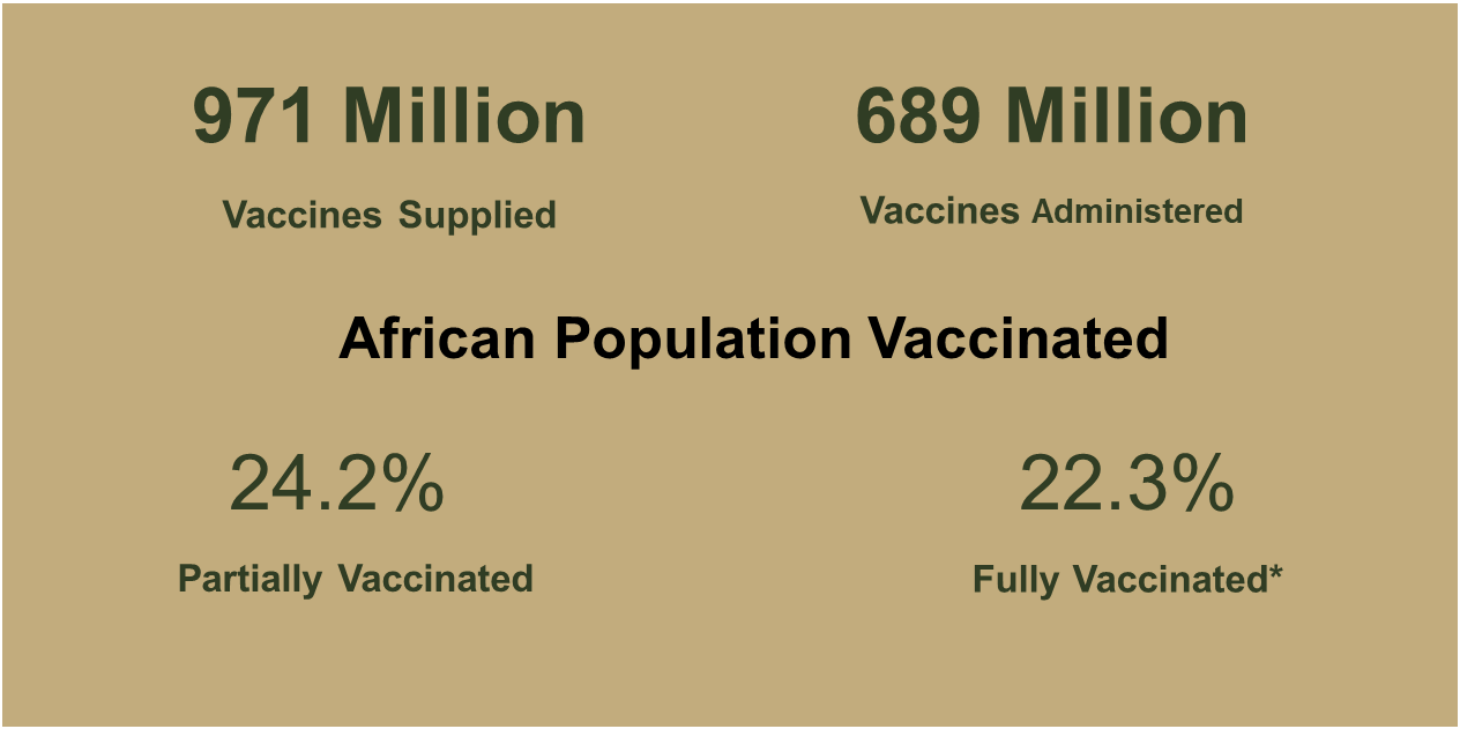
# COVID-19 Scientific and Public Health Policy Update[1] (28 September 2022)

*This bi-weekly 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 28 September 2022

**Note:**

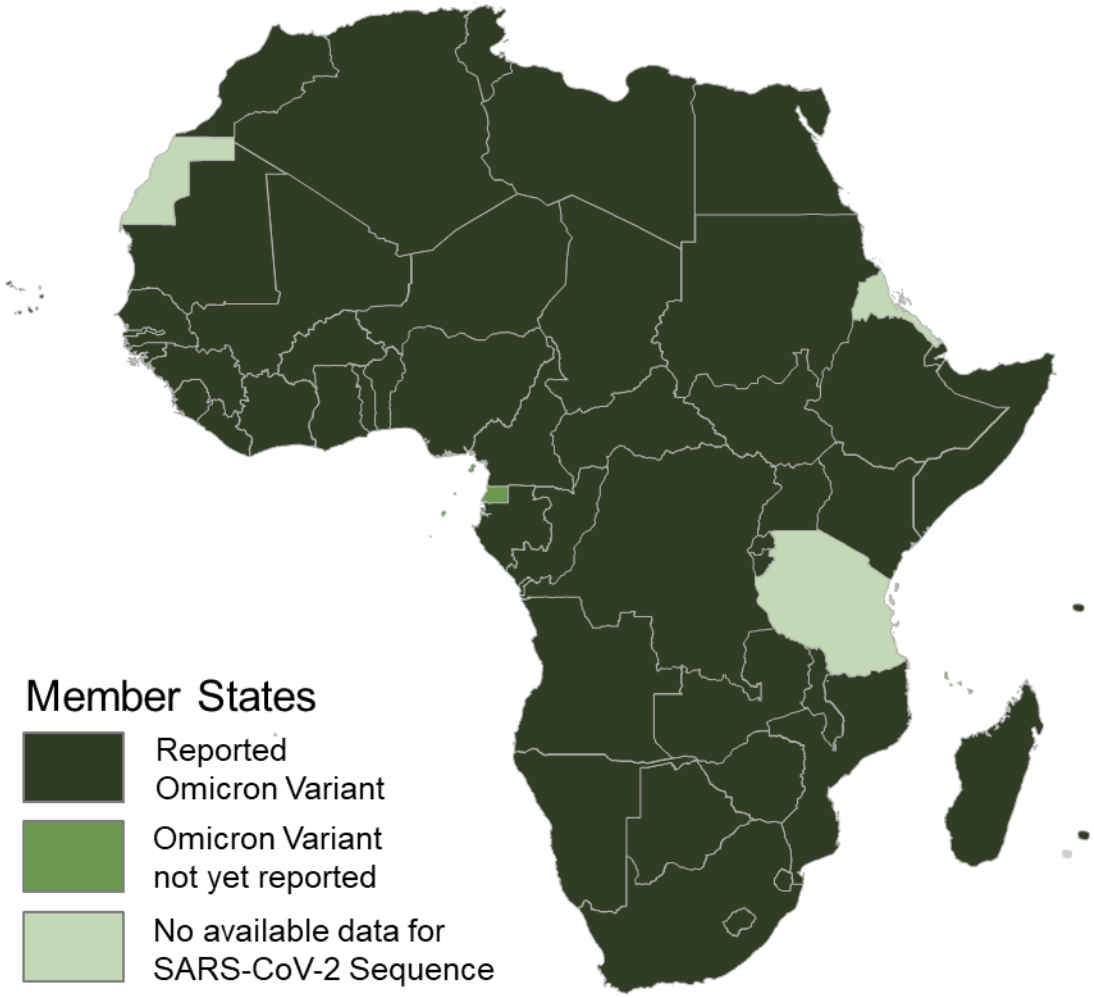
I. There is a reduction in figures (vaccines supplied) reported previously due to data cleaning.

II. Africa CDC has changed the denominator of the calculation for percentage fully vaccinated from 2020 population to 2022 population estimates (UNFPA) to give accurate projections from effective population size (Ne) perspectives. The resulting effect is that there will be a slight reduction in fully vaccinated coverage percentages of member states and the continent at large.

[1] This update compiled for use by African Union Member States and is developed collaboratively by the African Union-Africa CDC and World Health Organization - Regional Office for Africa. **This is a preliminary summary of information and does not represent policy decisions, recommendations, or final conclusions of the African Union- Africa CDC or WHO/AFRO**.

**Variants of Concern (VOC)**

The Omicron variant (B.1.1.529), first reported in South Africa on 24th November 2021, has spread to 198 countries/territories/areas worldwide. As of 28 September 2022, 51 (92.7%) of the 55 Member States in Africa have reported this variant. For more information visit https://africacdc.org/institutes/africa-pathogen-genomics-initiative/.




Updated 28 September 2022

## B. New guidelines and resources

**Since 13 Sept 2022,**

- Africa CDC[2] has published new guidance and resources on:
  - COVID-19 Test to Treat Guidelines for African Union Member States
  - Outbreak Brief 140: Coronavirus Disease 2019 (COVID-19) Pandemic

- U.S. CDC[3] has published new guidance and resources on:
  - Interim Infection Prevention and Control Recommendations for Healthcare Personnel During the COVID-19 Pandemic

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

- Interim Guidance for Managing Healthcare Personnel with SARS-CoV-2 Infection or Exposure to SARS-CoV-2
- Selected Adverse Events Reported after COVID-19 Vaccination
- CDC Strategy for Global Response to COVID-19 (2020-2023)

- WHO[4] has published new guidance and resources on:
  - Therapeutics and COVID-19: Living guideline, 16 September
  - Planning and budgeting tool for vaccine-preventable disease surveillance in priority countries for polio transition: user guide
  - Clinical management of COVID-19: Living guideline, 15 September
  - WHO policy brief: Maintaining infection prevention and control measures for COVID-19 in health care facilities
  - WHO policy brief: COVID-19 infodemic management
  - WHO policy brief: Building trust through risk communication and community engagement
  - WHO policy brief: Reaching COVID-19 vaccination targets
  - WHO policy brief: COVID-19 testing
  - WHO policy brief: Clinical management of COVID-19

- U.S. FDA[5] has issued press releases on:
  - On 27 September, FDA updated COVID-19 test policy, encourages developers to seek traditional premarket review for most test types
  - As of 27 September, 437 tests and sample collection devices are authorised by the FDA under emergency use authorisations (EUAs)

- ECDC[6] has issued new resources on:
  - The EU experience in the first phase of COVID-19: implications for measuring preparedness
  - Pilot protocol for a COVID-19 vaccine effectiveness study using health data registries

- UKHSA[7] has issued new guidance and press releases on:
  - Preventing and controlling outbreaks of COVID-19 in prisons and places of detention
  - National flu and COVID-19 surveillance reports published
  - National protocol for Comirnaty® Original/Omicron BA.1 (15/15 micrograms)/dose COVID-19 mRNA vaccine
  - Consensus statements and medium-term projections on COVID-19

## C. Scientific updates

### Basic Science

- This study assessed how the first 100,000 SARS-CoV-2 sequences from Africa have helped describe the pandemic on the continent, how this genomic surveillance in Africa has expanded, and how African countries adapted sequencing methods to deal with an evolving virus. The authors also highlight the impact that genomic sequencing in Africa has had on the global public health response, particularly through the identification and early analysis of new variants. They also describe how the Delta and Omicron variants have spread across the continent, and how their transmission dynamics were distinct from the Alpha and Beta variants. Sustained investment for diagnostics and genomic surveillance in Africa is needed as the virus continues to evolve. These investments are crucial for pandemic preparedness and response and will serve the health of the continent well into the 21st century.

[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

- This cohort study in Germany characterised serum neutralising activity of COVID-19 mRNA vaccine triple-immunized individuals who experienced Omicron BA.2 breakthrough infection compared to Omicron BA.1. The study included a total of 51 sera samples. Sera of individuals with BA.2 breakthrough infection were found to have broadly neutralising activity against previous variants of concern as well as all tested Omicron sub lineages, including BA.2 derived variants BA.2.12.1, BA.4/BA.5. Neutralisation of BA.2 and BA.4/BA.5 sub lineages by BA.2 convalescent sera is driven to a significant extent by antibodies targeting the N-terminal domain (NTD) of the spike glycoprotein. However, neutralisation by Omicron BA.1 convalescent sera depends exclusively on antibodies targeting the receptor binding domain (RBD). These findings suggest that exposure to Omicron BA.2, in contrast to BA.1 spike glycoprotein, triggers significant NTD specific recall responses in vaccinated individuals and thereby enhances the neutralisation of BA.4/BA.5 sub lineages. Given the current epidemiology with a predominance of BA.2 derived sub lineages like BA.4/BA.5 and rapidly ongoing evolution, these findings helped to inform development of their Omicron BA.4/BA.5-adapted vaccine.
- This study in the United States assessed factors associated with disease severity and survival in samples from 600 individuals hospitalised with COVID-19 during 2020. The authors found that severe disease and death were associated with altered antigen presentation signatures, as well as a distinct macrophage profile in the peripheral blood. They also studied lung macrophages, finding that those with severe COVID-19 had increased inflammatory monocytes and monocyte-derived macrophage infiltration, with a corresponding decrease in the alveolar macrophage population. Together, these results suggest that restoring macrophage homeostasis may be a strategy for treating COVID-19.

## Vaccines

- This cohort study in Austria assessed variant-specific humoral immunity after active and passive SARS-CoV-2 immunization in patients with haemato-oncologic diseases. The study involved 72 patients, 54 (75.0%) received a fourth vaccination (21 had solid tumours, and 33 had hematologic malignant neoplasms) and 18 (25.0%) received tixagevimab and cilgavimab as passive immunization. Median (range) anti-RBD levels increased in patients with haematological malignant neoplasms undergoing B cell–targeted therapy, particularly against Omicron sub-lineages BA.1 (before vs after fourth vaccination: 0.154 [0.059-1.556] optical density vs 0.969 [0.057-1.306] optical density; $p = 0.02$) and BA.4 (0.245 [0.052-1.270] optical density vs 0.966 [0.052-1.383] optical density; $p = 0.02$). There were no differences in antibody levels among patients with other haematological diseases. Similarly, there was a pronounced increase in median anti-RBD levels in patients with solid malignant neoplasms for all investigated variants of concern before vs after the fourth vaccination. Their findings suggest that passive immunization with tixagevimab and cilgavimab may not be effective in blocking Omicron sub lineages BA.1 and BA.4 (median inhibition of 99.9% for hu-1, 34.9% for BA.1, and 15.4% for BA.4 (Kruskal-Wallis $p < 0.001$).
- This case-control study in the United States assessed the odds of hospitalisation in adults who received COVID-19 mRNA booster immunization compared with vaccination with the primary mRNA vaccination series alone. The study included 3,062 cases and 12,248 matched controls who received either 2 or 3 doses of an mRNA COVID-19 vaccine and were hospitalised between October 2021 and July 2022 across 6 states. Factors associated with an increased odds of hospitalisation for COVID-19 included age of 70 years or older, male sex, cognitive disease, chronic obstructive pulmonary disease, diabetes, immunodeficiency, obesity, rheumatologic disease, transplant, and BNT162b2 (Pfizer-BioNTech) vaccine. Booster vaccination was associated with decreased odds of hospitalisation for COVID-19 (34.7% of cases vs 49.3% of matched controls; adjusted OR, 0.41 [95% CI, 0.37-0.46]). The odds of hospitalisation varied based on time since booster: less than 50 days (adjusted OR, 0.24 [95% CI, 0.18-0.30]), 50 to 100 days (adjusted OR, 0.24 [95% CI, 0.20-0.29]), 101 to 150 days (adjusted OR, 0.47 [95% CI, 0.38-0.58]), and longer than 150 days (adjusted OR, 0.72 [95% CI, 0.61-0.84]).
- This cohort study in Israel compared antibody waning after second and third BNT162b2 doses and estimated the association of antibody kinetics with susceptibility to infection with the Omicron variant of SARS-CoV-2. The study involved 4868 and 3972 health care workers who were followed up for 5 months after their second and third vaccine doses respectively. Waning of IgG levels was slower after

the third compared with the second dose (1.32%/d [95% CI, 1,29%/d to 1.36%/d] vs 2.26% [95% CI, 2.13%/d 2.38%/d]), as was waning of neutralising antibody levels (1.32%/d [95% CI, 1.21%/d to 1.43%/d] vs 3.34%/d [95% CI, 3.11%/d to 3.58%/d]). Among 2865 health care workers assessed for Omicron incidence during an additional 2 months of follow-up, lower IgG peak (ratio of means 0.86 [95% CI, 0.80-0.91]) was associated with Omicron infection, and among participants aged 65 years and older, faster waning of IgG and neutralising antibodies (ratio of mean rates, 1.40; [95% CI, 1.13-1.68] and 3.58 [95% CI, 1.92-6.67], respectively) were associated with Omicron infection.

- This test-negative case-control study in Canada estimated effectiveness of COVID-19 vaccines for preventing symptomatic infections due to the Omicron and Delta variants and severe outcomes (hospitalisation or death) associated with these infections. The study involved 134,435 participants (16,087 Omicron-positive cases, 4,261 Delta-positive cases, and 114,087 test-negative controls). Estimated vaccine effectiveness (VE) against symptomatic Delta infection decreased from 89% (95% CI, 86%-92%) 7 to 59 days after a second dose to 80% (95% CI, 74%-84%) after 240 or more days but increased to 97% (95% CI, 96%-98%) 7 or more days after a third dose. Estimated VE against symptomatic Omicron infection was 36% (95% CI, 24%-45%) 7 to 59 days after a second dose and 1% (95% CI, –8% to 10%) after 180 days or longer. However, 7 or more days after a third dose, it increased to 61% (95% CI, 56%-65%). Estimated VE against severe outcomes was high 7 or more days after a third dose for both Delta (99%; 95% CI, 98%-99%) and Omicron (95%; 95% CI, 87%-98%). Preventing infection due to Omicron and potential future variants may require tools beyond the currently available vaccines.
- This cross-sectional study in Belgium used a mixed-methods design to explore reasons people who were initially resistant to COVID-19 vaccines ended up getting vaccinated. The study involved 3171 fully vaccinated adults, of which 918 (29%) reported a low confidence level with COVID-19 vaccines. The most common reasons given for vaccination despite low confidence include: to facilitate travel (444 [48%]); recover freedom in day-to-day life (399 [44%]); 387 (42%) reported social pressure. Only 88 (10%) got vaccinated out of personal protection against COVID-19. Women and highly educated people were more likely to report the desire to avoid children's vaccination. Youths (aged 18-29 years) were more likely to be vaccinated for reasons related to individual liberty (facilitate travel/holiday; recover freedom) and social or professional pressure. qualitative analysis showed that "recovering freedom" and "escaping government constraints" were evoked by most respondents (55/86). Moral pressure from close contacts, the media, and government were mentioned by half of respondents (43). They reported feeling discriminated against and guilty, notably due to continuous recall of the government's announced vaccination target of 70% supposed to end the pandemic and the suspicion of being an "anti-vaxxer" or "conspiracist" if unvaccinated.

## Diagnostics

- None

## Care and Treatment

- This randomised clinical trial in Saudi Arabia and Kuwait assessed the effect of non-invasive ventilation delivered by helmet compared with usual respiratory support on the risk of mortality among adults with acute hypoxemic respiratory failure due to COVID-19. The study involved 320 adults across 8 sites. Patients were randomised (1:1) to receive helmet non-invasive ventilation or usual respiratory support (mask non-invasive ventilation, high-flow nasal oxygen, and standard oxygen). Within 28 days, 43/159 patients (27.0%) died in the helmet non-invasive ventilation group compared with 42/161 (26.1%) in the usual respiratory support group (risk difference, 1.0% [95% CI, −8.7% to 10.6%]; relative risk, 1.04 [95% CI, 0.72-1.49]; p = 0.85). Within 28 days, 75/159 patients (47.2%) required endotracheal intubation in the helmet non-invasive ventilation group compared with 81/161 (50.3%) in the usual respiratory support group (risk difference, −3.1% [95% CI, −14.1% to 7.8%]; relative risk, 0.94 [95% CI, 0.75-1.17]). There were no significant differences between the 2 groups in any of the prespecified secondary end points. Results of this study suggest that helmet non-invasive ventilation did not

significantly reduce 28-day mortality compared with usual respiratory support among patients with acute hypoxemic respiratory failure due to COVID-19 pneumonia.

- This cohort study in the United States assessed the risks and burdens of incident neurologic disorders at 12 months following acute SARS-CoV-2 infection. The study involved 154,068 people who had COVID-19, 5,638,795 contemporary controls and 5,859,621 historical controls, which altogether correspond to 14,064,985 person-years of follow up. In the post-acute phase of COVID-19, there was increased risk of an array of incident neurologic sequelae including ischemic and haemorrhagic stroke, cognition and memory disorders, peripheral nervous system disorders, episodic disorders (e.g., migraine and seizures), extrapyramidal and movement disorders, mental health disorders, musculoskeletal disorders, sensory disorders, Guillain–Barré syndrome, and encephalitis or encephalopathy. They found that the hazard ratio of any neurologic sequela was 1.42 (95% CI: 1.38, 1.47) and burden 70.69 (95% CI: 63.54, 78.01) per 1,000 persons at 12 months. The risks and burdens were elevated even in people who did not require hospitalisation during acute COVID-19. Their findings call for attention to the long-term neurologic consequences of SARS-CoV-2 infection.

## Epidemiology

- This cohort study in the United States assessed whether there was an increase in new diagnoses of type 1 diabetes (T1D) among paediatric patients after COVID-19. The study population included 1,091,494 paediatric patients: 314,917 with COVID-19 and 776,577 with non–COVID-19 respiratory infections. The matched cohort included 571 256 paediatric patients: 285,628 with COVID-19 and 285,628 with non–COVID-19 respiratory infections. By 6 months after COVID-19, 123 patients (0.043%) had received a new diagnosis of T1D, but only 72 (0.025%) were diagnosed with T1D within 6 months after non–COVID-19 respiratory infection. At 1, 3, and 6 months after infection, risk of diagnosis of T1D was greater among those infected with SARS-CoV-2 compared with those with non–COVID-19 respiratory infection (1 month: HR, 1.96 [95%CI, 1.26-3.06]; 3 months: HR, 2.10 [95% CI, 1.48-3.00]; 6 months: HR, 1.83 [95% CI, 1.36-2.44]). The increased risk of new-onset T1D after COVID-19 adds an important consideration for risk-benefit discussions for prevention and treatment of SARS-CoV-2 infection in paediatric populations.
- This study in Malawi assessed maternal and neonatal outcomes of pregnant and recently admitted pregnant patients with symptoms of COVID-19 and confirmed SARS-CoV-2 infection. The study involved 437 patients across 28 health facilities. SARS-CoV-2 infection was confirmed in 261 patients; of whom 76 (29%) had a severe maternal outcome and 45 (17%) died. These two outcomes were less common during the fourth wave (omicron dominance) than the second wave (adjusted OR of severe maternal outcome: 3.96 [95% CI 1.22–12.83], p=0.022; aOR of maternal death: 5.65 [1.54–20.69], p=0.0090) and the third wave (aOR: 3.18 [1.03–9.80], p=0.044; aOR: 3.52 [0.98–12.60], p=0.053). Shortness of breath was the only symptom associated with poor maternal outcomes of interest (p<0.0001), and was less frequently reported in the fourth wave (23%) than in the second wave (51%; p=0.0007) or third wave (50%; p=0.0004). The demographic characteristics and medical histories of patients were similar across the three waves. During the second and third waves, 12 (13%) of 92 singleton neonates were stillborn or died during maternal stay in the health-care facility of enrolment, compared with 0 of the 25 born in the fourth wave (p=0.067 *vs* preceding waves combined). Maternal and neonatal outcomes from COVID-19 in Malawi were less severe during the fourth wave compared to the preceding beta and delta waves.
- This prospective cohort study in China assessed the 2-year health outcomes among patients hospitalised for COVID-19. The study involved 1,864 patients who were available for both 1-year and 2-year follow-up visits at two COVID-19–designated hospitals in Wuhan. At 2-years after hospital discharge, 370 patients (19.8%) still had symptoms, including 224 (12.0%) with persisting symptoms and 146 (7.8%) with new-onset or worsening of symptoms. The most common symptoms were fatigue, chest tightness, anxiety, dyspnoea, and myalgia. Most symptoms resolved over time, but the incidence of dyspnoea showed no significant change (1-year vs 2-year, 2.6% [49 patients] vs 2.0% [37 patients]). A total of 116 patients (6.2%) had chronic obstructive pulmonary disease assessment test (CAT) total scores of at least 10 at 2-years after discharge. Patients who had been admitted to the intensive care

unit had higher risks of persistent symptoms (odds ratio, 2.69; 95% CI, 1.02-7.06; p = 0.04) and CAT scores of 10 or higher (odds ratio, 2.83; 95% CI, 1.21-6.66; p = 0.02). These results are related to the original strain of the virus, and their relevance to infections with the Omicron variant is not known.

- This nationwide cross-sectional study in the United States identified a distinct and significant temporal pattern of post-acute sequelae of SARS-CoV-2 (PASC) symptoms among survivors. The study involved 5652 PASC survivors who were randomly sorted into two independent samples for exploratory (EFA) and confirmatory factor analyses (CFA). Five factors emerged from the EFA: (1) cold and flu-like symptoms, (2) change in smell and/or taste, (3) dyspnoea and chest pain, (4) cognitive and visual problems, and (5) cardiac symptoms. The CFA had excellent model fit ($x^2$ = 513.721, df = 207, $p$ < 0.01, TLI = 0.952, CFI = 0.964, RMSEA = 0.024). These findings demonstrate a novel symptom pattern for PASC. These findings can enable nurses in the identification of at-risk patients and facilitate early, systematic symptom management strategies for PASC.
- This cross-sectional study in Poland assessed the relationship between previous exposure to *Borrelia* spp. and the risk of SARS-CoV-2 infection or severe COVID-19. Exposure to *Borrelia* was identified by multi-antigenic (19 antigens) serological testing of 87 patients: severe COVID-19 (n=31), asymptomatic to mild COVID-19 (n=28), and not infected with SARS-CoV-2 (n=28). Increased levels of *Borrelia*-specific IgGs strongly correlated with COVID-19 severity and risk of hospitalisation. These results suggest that a history of tick bites and related infections may contribute to the risks in COVID-19. Though mechanisms of this link are not clear yet, screening for antibodies targeting *Borrelia* may help accurately assess the odds of hospitalisation for SARS-CoV-2 infected patients, supporting efforts for efficient control of COVID-19.
- This randomised experimental study assessed people's willingness to provide their geospatial global positioning system (GPS) data from their Smartphone during the COVID-19 pandemic based on different methods of framing and incentives. The study involved 1055 participants from 41 countries on Amazon Mechanical Turk (MTurk), an online crowdsourcing platform. Participants living in India or in Brazil were more willing to provide their GPS data compared to those living in the United States. No significant differences were seen between positive and negative valence framing messages. Monetary incentives of $5 significantly increased participants' willingness to provide GPS data. Messaging that promotes altruistic donation with the addition of financial compensation will encourage the most active participation of users to provide private location data to fight the COVID-19 pandemic.
- This modelling study assessed how diverse sampling strategies in genomic sequencing may affect the estimation of key epidemiological parameters. The authors estimated basic reproduction number ($R_0$), time-varying effective reproduction number ($R_t$) and growth rate ($r_t$) from genomic sequencing data from Hong Kong and Amazonas state. Both $R_t$ and $r_t$ were found to be sensitive to changes in sampling whilst $R_0$ and the date of origin were relatively robust. Analysis using unsampled datasets result in the most biased $R_t$ and $r_t$ estimates for both the Hong Kong and Amazonas case studies. These results highlight the need for more targeted attempts at performing genomic surveillance and epidemic analyses particularly in resource-poor settings with limited genomic capability.

## Infection Prevention & Control

- None

## Non-pharmaceutical Interventions, Docial Distancing

- This study in France assessed the performance of commercially available community face masks (CFM) against standard medical face masks (MFM). The authors assessed the influence of the number of wash cycles, the water temperature and the possible use of detergent during the washing cycles on mask performance. The performance of the new and washed masks was characterized from the bacterial filtration efficiency (BFE) and the differential pressure (DP). The tests on the new masks showed that the MFM had always better BFE than CFMs. Although 2 (out of 10) of the CFMs showed a BFE value exceeding 95%, only one can be classified as type I MFM based on both BFE and DP requirements. The influence of the washing parameters was investigated on the MFM and these two

CFMs with excellent BFE properties. The parameters had no effect on the BFE of CFMs whilst the MFM exhibited a loss in efficiency when washed with detergent. The DP of masks were not impacted by the washing. The results clearly show that even though a compromise has to be made between the BFE and breathability, it seems possible to manufacture CFMs with performances similar to a type I MFM.

## D. Clinical Trials Updates

**Key updates:**

Vaccine trials:

- On 28 September 2022, Moderna announced the European Medicines Agency (EMA) has accepted a variation for the evaluation of a 50 µg booster dose of the Omicron-containing bivalent COVID-19 booster candidate, mRNA-1273.222 (Spikevax bivalent Original/Omicron BA.4-5) in adults 12 years and older. Spikevax bivalent Original/Omicron BA.4-5 is a next-generation bivalent vaccine that contains 25 µg of mRNA-1273 (Spikevax) and 25 µg of a vaccine candidate targeting the Omicron variant of concern (BA.4/BA.5). mRNA-1273.222 targets both the original strain of SARS-CoV-2 as well as the BA.4/BA.5 subvariants of the Omicron strain. Moderna's submission to the EMA is based on preclinical data for mRNA-1273.222 as well as clinical trial data from a Phase 2/3 studying Spikevax bivalent Original/Omicron BA.1 (mRNA-1273.214), a bivalent booster vaccine targeting the Omicron BA.1 subvariant, which recently received EMA approval. Clinical trial registration #: (NCT05249829).
- On 26 September 2022, Pfizer and BioNTech announced they have completed a submission to the U.S. Food and Drug Administration (FDA) requesting Emergency Use Authorization (EUA) of a 10-µg booster dose of the Omicron BA.4/BA.5-adapted bivalent COVID-19 vaccine for children ages 5 through 11 years of age. The request is supported by safety and immunogenicity data from the bivalent Omicron BA.1-adapted vaccine, non-clinical and manufacturing data from the 10-µg bivalent Omicron BA.4/BA.5-adapted vaccine, and pre-clinical data from the Omicron BA.4/BA.5-adapted vaccine in their decision. Phase 1/2/3 study has been initiated to evaluate the safety, tolerability, and immunogenicity of different doses and dosing regimens of the Omicron BA.4/BA.5-adapted bivalent COVID-19 vaccine in children 6 months through 11 years of age. Clinical trial registration #: (NCT05543616).
- On 20 September 2022, Moat Biotechnology announces promising initial Phase 1 trial results of an intranasal COVID-19 vaccine which utilizes the novel second generation single-cycle adenovirus vaccine platform (SC-AdVax). The novel SC-AdVax platform targets cells in the respiratory tract or gastrointestinal tract to elicit a strong mucosal immune response by reacting to pathogens at their point of entry. The Phase 1 clinical trial is being performed in Australia, and the COVID-19 vaccine was safe and well tolerated in the initial ascending dose cohorts. In addition, when the vaccine was given as a boost to subjects receiving a previous mRNA COVID-19 vaccine, strong mucosal and systemic neutralising antibody responses, and a systemic Th1-skewed T cell response against the SARS-CoV-2 spike protein was observed in a majority of subjects.
- On 16 September 2022, Novavax announced the submission of a request to the World Health Organization (WHO) to update the Emergency Use Listing (EUL) of Nuvaxovid (NVX-CoV2373) COVID-19 vaccine for active immunization to prevent COVID-19 as a homologous and heterologous booster in adults aged 18 and older. The request is supported by data from Novavax' Phase 2 trial conducted in Australia, from a separate Phase 2 trial conducted in South Africa, and from the UK-sponsored COV-BOOST trial. As part of the Phase 2 trials, a single booster dose of Nuvaxovid was administered to healthy adult participants approximately six months after their primary two-dose vaccination series of Nuvaxovid. The third dose produced increased immune responses comparable to or exceeding levels associated with protection in Phase 3 clinical trials. In the COV-BOOST trial, Nuvaxovid induced a meaningful antibody response when used as a heterologous third booster dose. Clinical trial registration #: (NCT05372588).

Therapeutics trials:

- On 21 September 2022, Adamis Pharmaceuticals announced the third planned interim analysis of the Phase 2/3 clinical trial examining the effects of Tempol in high risk subjects with early COVID-19 infection did not achieve its primary endpoint, as measured by comparing the rate of sustained clinical

resolution of symptoms of COVID-19 at day 14 of Tempol versus placebo. The trial "A Phase 2/3, Adaptive, Randomised, Double-Blind, Placebo-Controlled Study to Examine the Effects of Tempol (MBM-02) in Subjects With COVID-19 Infection" was designed to enrol approximately 248 high risk subjects with early COVID-19 infection age 18 years of age and older. Eligible subjects with positive COVID-19 infection within five days of study entry plus at least one co-morbidity were randomised one-to-one to receive either Tempol or placebo. Co-morbidities include age of 65 or older, hypertension, diabetes, obesity, cancer, immunodeficiency and in the opinion of the investigator the risk factor is not acutely life-threatening. Patients randomised to Tempol received 800mg daily in two divided oral doses of 400mg capsules for up to 21 days. Similarly, placebo capsules were administered twice daily to subjects in the placebo group for up to 21 days. The independent Data Safety Monitoring Board (DSMB) recommended that the study be halted early due to lack of efficacy. The DSMB did note that no safety concerns were identified in the subjects that received Tempol. Based on the recommendation from the DSMB, the trial has been halted and will now evaluate the unblinded data from the trial to determine the next developmental steps for Tempol. Clinical trial registration #: (NCT04729595).

Immunotherapies trials:

- On 20 September 2022, AstraZeneca's Evusheld (tixagevimab and cilgavimab, formerly AZD7442), a long-acting antibody combination, has been approved in the European Union (EU) for the treatment of adults and adolescents (aged 12 years and older weighing at least 40 kg) with COVID-19 who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID 19. The approval based on results from the TACKLE Phase 3 COVID-19 treatment trial which showed one intramuscular (IM) dose of Evusheld provided clinically and statistically significant protection against progression to severe COVID-19 or death from any cause compared to placebo. Evusheld treatment earlier in the disease course led to more favourable outcomes. TACKLE was conducted in non-hospitalised adults with mild-to-moderate COVID-19 who were symptomatic for seven days or less. 90% of trial participants were at high risk of progression to severe COVID-19 due to co-morbidities or age. Evusheld was generally well tolerated in the trial. Clinical trial registration #: (NCT05438498)
- On 16 September 2022, AstraZeneca reported that Evusheld (tixagevimab and cilgavimab, formerly AZD7442), a long-acting antibody combination, has been recommended for marketing authorisation in the European Union (EU) for the treatment of adults and adolescents (aged 12 years and older weighing at least 40 kg) with COVID 19 who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID 19. The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency based its positive opinion on results from the TACKLE Phase 3 randomised, double-blind, placebo-controlled, multi-centre trial, assessing the safety and efficacy of a single 600mg IM dose of Evusheld (300mg each of cilgavimab and tixagevimab) compared to placebo for the treatment of mild-to-moderate COVID-19. 903 participants who were adults 18 years-old and over with mild-to-moderate COVID-19 and were symptomatic for seven days or less were randomised (1:1) to receive either Evusheld (n = 452) or saline placebo (n = 451), administered in two separate, sequential IM injections. The trial demonstrated that one intramuscular (IM) dose of Evusheld provided clinically and statistically significant protection against progression to severe COVID-19 or death from any cause compared to placebo. Evusheld treatment earlier in the disease course led to more favourable outcomes. TACKLE was conducted in non-hospitalised adults with mild-to-moderate COVID-19 who were symptomatic for seven days or less. 90% of trial participants were at high risk of progression to severe COVID-19 due to co-morbidities or age. Evusheld was generally well tolerated in the trial. Clinical trial registration #: (NCT05438498)
- On 16 September 2022, Gilead Sciences announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion to extend the indication of Veklury (remdesivir) for the treatment of paediatric patients (weighing at least 40 kg) who do not require supplemental oxygen and are at increased risk of progressing to severe COVID-19 and paediatric patients (4 weeks of age and older and weighing at least 3 kg) with SARS-CoV-2 with pneumonia who require supplemental oxygen (low- or high-flow oxygen or other non-invasive ventilation at the start of treatment). The positive opinion based on results from the ongoing CARAVAN Phase 2/3 study, which demonstrated Veklury was generally well-tolerated among paediatric patients

hospitalised with COVID-19, with a high proportion of participants showing clinical improvement and recovery, as well as data from trials in adults. Of the 53 paediatric patients enrolled in the CARAVAN study, no new safety signals were apparent for patients treated with Veklury. Overall, 75% and 85% showed clinical improvement (≥2 point increase on an 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, which were consistent with the patients' underlying medical conditions prior to study entry or with COVID-19 during hospitalisation. Clinical trial registration #: (NCT04431453).

- On 15 September 2022, Gilead Sciences announced updates to the World Health Organization's (WHO) Therapeutics and COVID-19: living guideline, which now conditionally recommends Veklury (remdesivir) for the treatment of patients with severe COVID-19 and continues to conditionally recommend Veklury in those with non-severe COVID-19 at the highest risk of hospitalisation. The recommendation based on WHO-sponsored SOLIDARITY study, which showed a statistically significant 17% lower relative risk of death or progression to needing ventilation in patients requiring supplemental oxygen at baseline, compared to standard of care (RR: 0.83; 95% CI: 0.75–0.93). Additionally, SOLIDARITY showed a statistically significant 13% lower relative risk of mortality with Veklury treatment for those patients hospitalised on supplemental oxygen and not requiring mechanical ventilation, compared with standard of care (RR: 0.87; 95% CI: 0.76–0.99). In the study, Veklury had no significant effect on patients with COVID-19 who were already being ventilated. Clinical trial registration #: (NCT04575064)
- On 15 September 2022, Omeros reported results from the narsoplimab arm of the I-SPY COVID Trial, which analysis in the randomised patient population shows that the addition of narsoplimab to treatment of critically ill patients with COVID-19 reduces the mortality risk (hazard ratio [HR]=0.81, with probability [HR <1] equal to 0.77). Narsoplimab showed the largest reduction in mortality risk to date across all drugs reported from the I-SPY COVID Trial. There were 91 patients randomised to the narsoplimab arm of the trial across 27 participating US sites. The 91 randomised patients were compared to the 116 patients concurrently randomised to the control arm. All patients received standard of care including dexamethasone and remdesivir. Bayesian statistics were prespecified and employed for analyses. Narsoplimab was to be administered at a dose of 4 mg/kg given as a 30-minute intravenous infusion (up to a maximum of 370 mg per infusion) twice weekly for the earlier of a total of 4 weeks (i.e., 9 doses) or until hospital discharge. However, in approximately half of the patients who died in the narsoplimab group, narsoplimab was not given or was prematurely stopped, with those patients dying 9 to 35 days later. Despite narsoplimab treatment exposure in a limited number of patients in this trial, a substantial efficacy signal was observed in reducing the risk of mortality for critically ill COVID-19 patients. Narsoplimab was not observed to shorten the time to recovery in critically ill patients with COVID-19 in this study. The study did not identify any new safety signals for narsoplimab in the setting of critically ill COVID-19 patients. Clinical trial registration #: (NCT04488081).
- On 14 September 2022, eFFECTOR Therapeutics announced it has dosed the first patient in the second cohort of its Phase 1b clinical trial of zotatifin in non-hospitalised adults with confirmed COVID-19 infection. The study is a double-blind, randomised, placebo-controlled trial evaluating the safety and antiviral activity of a single dose of zotatifin and is being conducted in collaboration with the Quantitative Biosciences Institute (QBI) at the University of California and San Francisco. Zotatifin is a potent and sequence-selective small molecule inhibitor of eIF4A, a host protein required to unwind the complex secondary structures within the 5' untranslated region of the genome of SARS-CoV-2 and other RNA viruses. Inhibiting the activity of eIF4A prevents the translation of the viral polyprotein needed for replication of the virus. Clinical trial registration #: (NCT04632381).

## Contributors

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