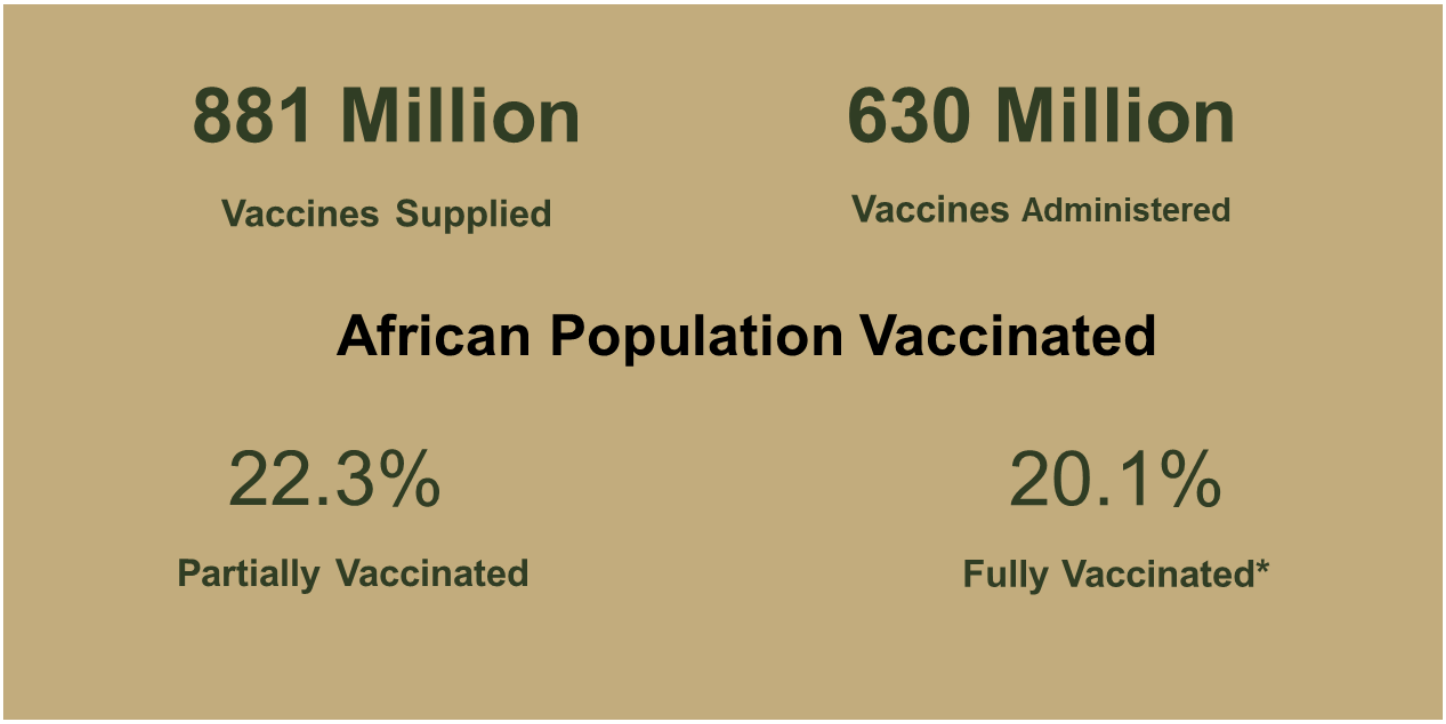
COVID-19 Scientific and Public Health Policy Update[1] (20 July 2022)

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 20 July 2022

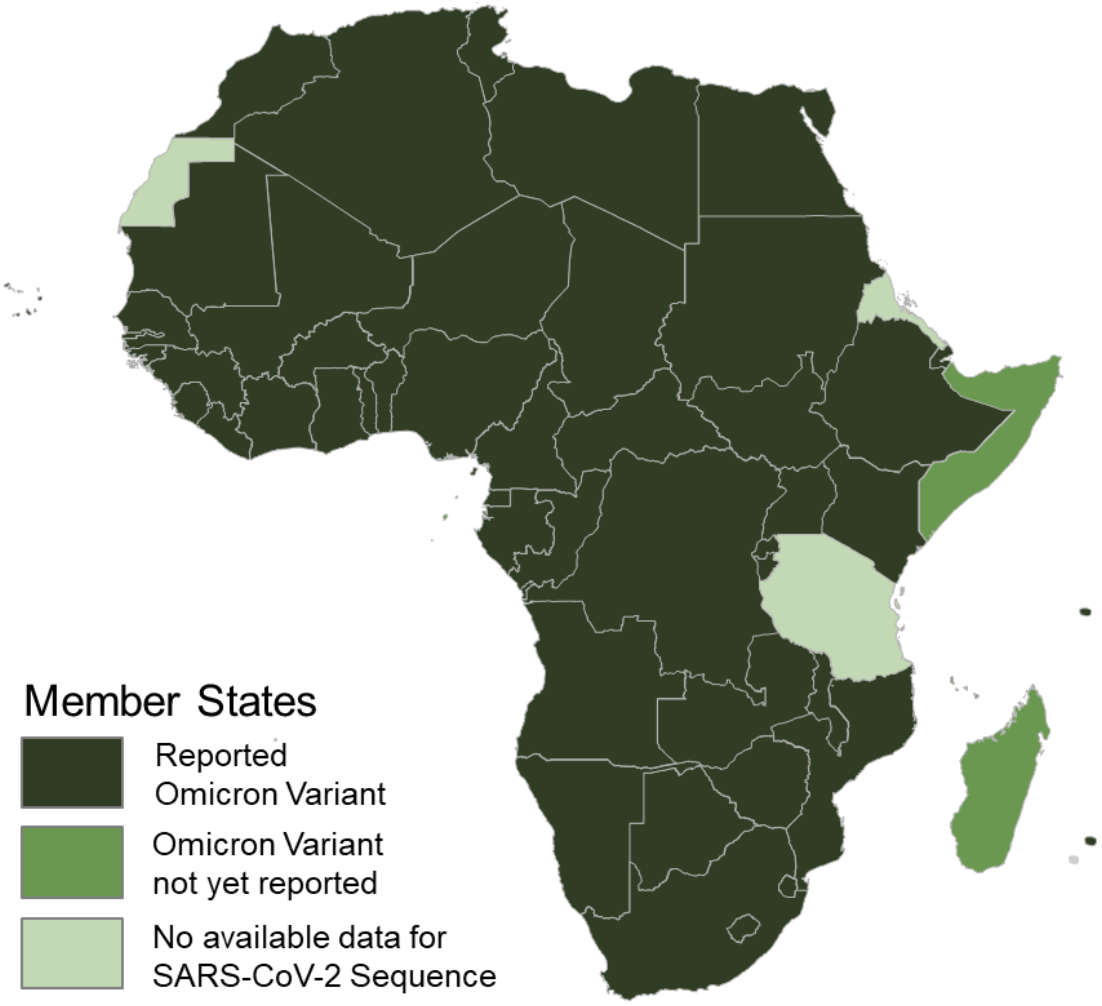
Note: Africa CDC has changed the denominator of the calculation for percentage fully vaccinated from 2020 population to 2022 population estimates (UNFPA) to give accurate projections from effective population size (Ne) perspectives.

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 20 July 2022, 50 (90.9%) of the 55 Member States in Africa have reported this variant. For more information visit https://africacdc.org/institutes/africa-pathogen-genomics-initiative/.



Updated 20 July 2022

B. New guidelines and resources

Since 5 July 2022,

- Africa CDC[2] has published new guidance and resources on:
  - Outbreak Brief 130: Coronavirus Disease 2019 (COVID-19) Pandemic
  - Africa CDC – Mastercard Foundation: Saving Lives and Livelihoods Newsletter, June 2022

- U.S. CDC[3] has published new guidance and resources on:
  - Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19
  - Selected Adverse Events Reported after COVID-19 Vaccination
  - Social Media Toolkit: COVID-19 Vaccines for Children/Teens

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

- New COVID-19 Vaccine Effectiveness Data Showcase Protection Gained by 3rd and 4th Doses

- WHO[4] has published new guidance and resources on:
  - Therapeutics and COVID-19: living guideline
  - Contact tracing and quarantine in the context of COVID-19: interim guidance
  - Western Pacific Regional road map for COVID-19 vaccination response 2021-2022

- U.S. FDA[5] has issued press releases on:
  - On 13 July, FDA authorized emergency use of Novavax COVID-19 Vaccine, adjuvanted
  - On 8 July, FDA approved COMIRNATY for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 through 15 years of age
  - On 6 July, FDA authorized Pharmacists to prescribe Paxlovid with certain limitations
  - As of 19 July, 441 tests and sample collection devices are authorised by the FDA under emergency use authorisations (EUAs)

- ECDC[6] has issued new resources on:
  - Preliminary public health considerations for COVID-19 vaccination strategies in the second half of 2022
  - Operational considerations for respiratory virus surveillance in Europe
  - COVID-19 Contact tracing: country experiences and way forward

- UKHSA[7] has issued new guidance and press releases on:
  - Over 50s to be offered COVID-19 booster and flu jab this autumn
  - COVID-19 therapeutic agents: technical briefings
  - Assessment and procurement of coronavirus (COVID-19) tests

C. Scientific updates

Basic Science

- This single-centre, prospective cohort study in Italy assessed the long-term anti–SARS-CoV-2 spike receptor-binding domain (S-RBD) IgG kinetics in children after SARS-CoV-2 infection. The study involved a cohort of 252 COVID-19 family clusters who underwent serologic follow-up at 1 to 4, 5 to 10, and more than 10 months after infection with quantification of anti–S-RBD IgG by chemiluminescent immunoassay. The patients were enrolled from 1 April 2020, to 31 August 31 2021. Among 697 cases, 674 (96.7%) were asymptomatic or mild. Children had significantly higher S-RBD IgG titres than older patients across all follow-up time points, with an overall median S-RBD IgG titre in patients younger than 3 years 5-fold higher than adults (304.8 [IQR, 139.0-516.6] kBAU/L vs 55.6 [24.2-136.0] kBAU/L, $p < 0.001$). Longitudinal analysis of 56 study participants sampled at least twice during follow-up demonstrated the persistence of antibodies up to 10 months from infection in all age classes, despite a progressive decline over time. These results provide further evidence of sustained immune response in children up to 1 year after primary SARS-CoV-2 infection.
- This retrospective cohort study in the United States assessed the effect of antecedent serum lipid levels on SARS-CoV-2 infection risk. The study involved 11,001 individuals in the Arkansas Clinical Data-repository. Among them, 1340 (12.2%) tested positive for COVID-19. The highest trajectory for antecedent serum high-density lipoprotein-cholesterol (HDL-C) was associated with the lowest SARS-CoV-2 infection risk (RR 0.63, 95%CI 0.46-0.86). Antecedent serum low-density lipoprotein-cholesterol

[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

(LDL-C), total cholesterol (TC), and triglycerides (TG) were not independently associated with SARS-CoV-2 infection risk. In COVID-19 patients, serum HDL-C (-7.7, 95%CI -9.8 to -5.5 mg/dL), and LDL-C (-6.29, 95%CI -12.2 to -0.37 mg/dL), but not TG levels, decreased transiently at the time of testing. Further studies are needed to determine the potential role of lipid-modulating therapies in the prevention and management of COVID-19.

Vaccines

- This retrospective cohort study in Argentina assessed vaccine effectiveness (VE) against COVID-19-associated-hospitalisations in the 3–17-year old population during the Omicron outbreak. The study involved 1,536,435 individuals who had received zero or two doses of SARS-CoV-2 vaccines. Of the latter, 1,440,389 were vaccinated and 96,046 not vaccinated. mRNA-1273 and BNT162b2 were administered to 12–17-year-old subjects; and BBIBP-CorV to 3–11-year subjects. VE were 78.0% [95% CI: 68.7–84.2], 76.4% [95% CI: 62.9–84.5] and 80.0% [95% CI: 64.3–88.0] for the entire cohort, 3–11-year-old (BBIBP-CorV) subgroup and 12–17 (mRNA vaccines) subgroup, respectively. VE for the entire population was 82.7% during the period of Delta and Omicron overlapping circulation and decreased to 67.7% when Omicron was the only variant present. Application of a booster dose in children aged 3–11 years warrants further consideration.
- This retrospective cohort study in the United States assessed adverse events and health impacts associated with simultaneously administered COVID-19 mRNA booster and seasonal influenza vaccines. The study involved 981,099 individuals ≥12 years registered with v-safe, of which 92,023 (9.4%) reported to receive simultaneous doses of COVID-19 mRNA booster and seasonal influenza vaccines. In the week following vaccination, any systemic reactions were reported by 58.9% (36,144/61,390) of respondents who simultaneously received Pfizer-BioNTech booster and influenza vaccines and 68.6% (21,027/30,633) of respondents who simultaneously received Moderna booster and influenza vaccines. Respondents who simultaneously received influenza and Pfizer-BioNTech booster vaccines (aOR, 1.08; 95% CI, 1.06-1.10) or influenza and Moderna booster vaccines (aOR, 1.11; 95% CI, 1.08-1.14) were slightly more likely to report any systemic reaction in the week following simultaneous vaccination than respondents who received only a COVID-19 mRNA vaccine booster.
- This test-negative case-control study in the United States assessed the effectiveness of maternal vaccination against hospitalisation for COVID-19 among infants younger than 6 months of age. The study involved 537 case infants (with COVID-19) and 512 control infants (without COVID-19) across 30 hospitals in 22 states. Proportions of infants born to mothers who had been fully vaccinated against COVID-19 during pregnancy were 16% and 29% in the cases and controls respectively. Among the case infants, 113 (21%) received intensive care (64 [12%] received mechanical ventilation or vasoactive infusions). Two case infants died from COVID-19; neither infant's mother had been vaccinated during pregnancy. The effectiveness of maternal vaccination against hospitalisation for COVID-19 among infants was 52% (95% CI, 33 to 65) overall, 80% (95% CI, 60 to 90) during the delta period, and 38% (95% CI, 8 to 58) during the omicron period. Effectiveness was 69% (95% CI, 50 to 80) when maternal vaccination occurred after 20 weeks of pregnancy and 38% (95% CI, 3 to 60) during the first 20 weeks of pregnancy. These findings provide additional support for the current recommendations regarding COVID-19 vaccination during pregnancy.
- This national, matched, test-negative, case–control study in Qatar assessed the effectiveness of vaccination with BNT162b2 or mRNA-1273, natural immunity due to previous infection with variants other than omicron, and hybrid immunity against symptomatic omicron infection and against severe, critical, or fatal COVID-19. The effectiveness of previous infection alone against symptomatic BA.2 infection was 46.1% (95% CI, 39.5 to 51.9). The effectiveness of vaccination with 2 doses of BNT162b2 and no previous infection was negligible (−1.1%; 95% CI, −7.1 to 4.6), but nearly all persons had received their second dose more than 6 months earlier. The effectiveness of 3 doses of BNT162b2 and no previous infection was 52.2% (95% CI, 48.1 to 55.9). The effectiveness of previous infection and 2 doses of BNT162b2 was 55.1% (95% CI, 50.9 to 58.9), and the effectiveness of previous infection and 3 doses of BNT162b2 was 77.3% (95% CI, 72.4 to 81.4). Previous infection alone, BNT162b2 vaccination alone, and hybrid immunity all showed strong effectiveness (>70%) against severe, critical,

or fatal COVID-19 due to BA.2 infection. The authors observed similar results for effectiveness against BA.1 infection and of vaccination with mRNA-1273.

Diagnostics

- This multi-centre laboratory evaluation study in Australia describes the development and validation of the *in vitro* and clinical performance of salivary swab RT-PCR for implementation of SARS-CoV-2 surveillance testing. The agreement of self-collected saliva swabs for RT-PCR was 84.5% (95% CI 68.6 to 93.8) compared to RT-PCR using nasal/oropharyngeal swab samples collected by a healthcare practitioner, when saliva samples were collected within seven days of symptom onset. Between 7th December 2020 and 17th December 2021, almost 500,000 RT-PCR tests were performed on saliva swabs self-collected by 102 staff working in quarantine hotels in Melbourne. Of these, 20 positive saliva swabs were produced by 13 staff (0.004%). The majority of staff that tested positive occurred during periods of community transmission of the SARS-CoV-2 Delta variant. These results demonstrate the feasibility of widespread pooled salivary swab RT-PCR surveillance and applicability of this approach across a range of laboratory testing platforms.
- This study in China describes the development and performance benchmarking of an inexpensive (approximately US $0.30 per test) assay for the rapid (sample-to-answer time within 30 min) colorimetric detection of SARS-CoV-2 variants. The assay, which was integrated into foldable paper strips, leverages nucleic acid strand-displacement reactions, the thermodynamic energy penalty associated with single-base-pair mismatches and the metal-ion-controlled enzymatic cleavage of urea to amplify the recognition of viral RNAs for the colorimetric readout of changes in pH via a smartphone. For 50 throat swab samples, the assay simultaneously detected the presence of SARS-CoV-2 and mutations specific to the SARS-CoV-2 variants Alpha, Beta and Gamma, with 100% concordance with real-time quantitative polymerase chain reaction and RNA sequencing. Customizable and inexpensive paper-based assays for the detection of viruses and their variants may facilitate viral surveillance.
- This study in China describes the development and performance of a cost-effective modular microfluidic reverse transcription (RT)-PCR and RT-loop mediated isothermal amplification (RT-LAMP) platform, Epidax®, for the point-of-care testing and confirmation of SARS-CoV-2. The platform is versatile and can be reconfigured either for screening using endpoint RT-PCR or RT-LAMP tests or for confirmatory tests using real-time RT-PCR. The platform is highly sensitive and detects as little as one RNA copy per µL for real-time and endpoint RT-PCR, while using only half of the reagents. The authors achieved comparable results with those of a commercial platform when detecting SARS-CoV-2 viruses from 81 clinical RNA extracts. Epidax® can also detect SARS-CoV-2 from 44 nasopharyngeal samples without RNA extraction by using a direct RT-PCR assay, which shortens the sample-to-answer time to an hour with minimal user steps. Furthermore, they validated the technology using an RT-LAMP assay on 54 clinical RNA extracts. Overall, their platform provides a sensitive, cost-effective, and accurate diagnostic solution for low-resource settings.

Care and Treatment

- This propensity score–matched cohort study and randomised comparative effectiveness trial in the United States assessed the effectiveness of casirivimab-imdevimab and sotrovimab against the Delta variant. A total of 3,069 patients (1,023 received monoclonal antibody [mAb] treatment, 2,046 had no mAb treatment) were included in the prospective cohort study, and 3,558 patients were included in the randomised comparative effectiveness trial. In propensity score–matched models, mAb treatment was associated with reduced risk of hospitalisation or death (RR, 0.40; 95% CI, 0.28-0.57) compared with no treatment. Both casirivimab-imdevimab (RR, 0.31; 95% CI, 0.20-0.50) and sotrovimab (RR, 0.60; 95% CI, 0.37-1.00) were associated with reduced hospitalisation or death compared with no mAb treatment. In the clinical trial, 2,454 patients were randomised to receive casirivimab-imdevimab and 1,104 patients were randomised to receive sotrovimab. The median (IQR) hospital-free days were 28 (28-28) for both mAb treatments, the 28-day mortality rate was less than 1% (n = 12) for casirivimab-imdevimab and less than 1% (n = 7) for sotrovimab, and the hospitalisation rate by day 28 was 12%

(n = 291) for casirivimab-imdevimab and 13% (n = 140) for sotrovimab. Compared with patients who received casirivimab-imdevimab, those who received sotrovimab had a median adjusted OR for hospital-free days of 0.88 (95% CI, 0.70-1.11). This OR yielded 86% probability of inferiority for sotrovimab vs casirivimab-imdevimab and 79% probability of equivalence. Findings of this study suggest that casirivimab-imdevimab and sotrovimab were both associated with reduced risk of hospitalisation or death and had similar effectiveness, although they did not meet the prespecified criteria for statistical inferiority or equivalence.

- This secondary data analysis of a cluster randomised clinical trial in the United States assessed drug-drug interactions (DDIs) between nirmatrelvir-ritonavir and potentially inappropriate medications (PIMs) in older adults with polypharmacy. The study involved 5,698 adults ≥65 years who were taking 5 or more medications. Of 5698 patients, 3869 (67.9%) received at least 1 interacting medication prescription. The most common DDIs were with antithrombotic medications (2131 [37.4%]) or statins (1901 [33.4%]). Among the 3869 patients with interacting medication prescriptions, 823 (21.3%) had at least 1 PIM, of whom 627 (76.2%) had a high-risk DDI with nirmatrelvir-ritonavir. Common deprescribing opportunities included dual anticoagulant therapy without a recent coronary event or intervention (200/489 [41.0%]), alfuzosin or tamsulosin for benign prostatic hypertrophy in a person with orthostatic hypotension or recurrent falls (174/779 [22.3%]), and antipsychotics for sleep or agitation (62/274 [22.6%]).
- This randomised, double-blind, multicentre, parallel group, placebo-controlled phase III clinical trial in India assessed the ability of nitric oxide (NO) to rapidly eradicate nasal SARS-CoV-2 RNA. The study involved 306 adults with mild symptomatic COVID-19, the participants were randomised in a 1:1 to receive nitric oxide nasal spray (NONS) (*N* = 153) vs placebo (*N* = 153). NONS was self-administered six times daily as two sprays per nostril (0.45 mL of solution/dose) for seven days. Overall, mean SARS-CoV-2 RNA concentrations (6.96 log10 copies/mL in the NONS group and 7.16 log10 copies/mL in the placebo group) were comparable at baseline. Primary endpoint mean treatment difference SARS-CoV-2 RNA change from baseline to the end of treatment (EOT) was -0.52 copies/mL (SE 0.202, 95% CI -0.92 to -0.12; p = 0.010) with NONS compared to placebo. Secondary endpoint assessments demonstrated a greater proportion of patients receiving NONS (82.8%) cleared SARS-CoV-2 (RT-PCR negative) by EOT compared to placebo (66.7%, p = 0.046), with no virus RNA detected a median of four days earlier compared to placebo (three vs seven days; p = 0.044).
- This randomised, double-blind, phase 3, placebo-controlled trial in the United States, Europe, Uganda and Singapore assessed the efficacy of tixagevimab–cilgavimab in patients who are hospitalised with COVID-19. The study involved 1455 adults across 81 sites who were randomly assigned in a 1:1 ratio to receive intravenous tixagevimab 300 mg–cilgavimab 300 mg or placebo, in addition to remdesivir and other standard care. The estimated cumulative incidence of sustained recovery was 89% for tixagevimab–cilgavimab and 86% for placebo group participants at day 90 in the full cohort (recovery rate ratio [RRR] 1.08 [95% CI 0.97–1.20]; p=0.21). Results were similar in the seronegative subgroup (RRR 1.14 [0.97–1.34]; p=0.13). Mortality was lower in the tixagevimab–cilgavimab group (61 [9%]) versus placebo group (86 [12%]; hazard ratio [HR] 0.70 [95% CI 0.50–0.97]; p=0.032). The composite safety outcome occurred in 178 (25%) tixagevimab–cilgavimab and 212 (30%) placebo group participants (HR 0·83 [0.68–1.01]; p=0.059). Serious adverse events occurred in 34 (5%) participants in the tixagevimab–cilgavimab group and 38 (5%) in the placebo group. Among patients hospitalised with COVID-19 receiving remdesivir and other standard care, tixagevimab–cilgavimab did not improve the primary outcome of time to sustained recovery but was safe and mortality was lower.

Epidemiology

- This population-based cohort study in Germany developed and validated an easy-to-use Post-COVID Syndrome (PCS) severity score. The study included 1,442 adults with PCR confirmed SARS-CoV-2 infection across three German regions (Kiel, Berlin, Würzburg) between November 2020 and September 2021. In Kiel-I (*n* = 667, 57% women), 90% of participants had received outpatient treatment for acute COVID-19. Neurological ailments (61.5%), fatigue (57.1%), and sleep disturbance (57.0%) were the most frequent persisting symptoms at 6–12 months after infection. Across sub-cohorts

(Würzburg/Berlin, *n* = 316, 52% women; Kiel-II, *n* = 459, 56% women), higher PCS scores were associated with lower health-related quality of life (EQ-5D-5L-VAS/-index: *r* = -0.54/ -0.56, all *p* < 0.0001). Severe, moderate, and mild/no PCS according to the individual participant's PCS score occurred in 18.8%, 48.2%, and 32.9%, respectively, of the Kiel-I sub-cohort. In both validation sub-cohorts, statistically significant predictors of the PCS score included the intensity of acute phase symptoms and the level of personal resilience. The PCS score developed holds promise to facilitate the clinical diagnosis of PCS, scientific studies of its natural course, and the development of therapeutic interventions.

- This retrospective study in the United States assessed the association of COVID-19 and atrial fibrillation (AF) or atrial flutter (Afl) in hospitalised adult patients. The study involved 11,004 COVID-19 negative patients who were matched to 3,090 COVID-19 positive patients and 5005 pre-pandemic patients matched to 2283 COVID-19 positive patients. COVID-19 positive patients had 1.19 times the odds (95% CI 1.00, 1.41) of developing AF compared to COVID-19 negative patients and 1.57 times the odds (95% CI 1.23, 2.00) of developing AF compared to pre-pandemic patients. Their study demonstrated an increased risk for AF, directing the attention for improved screening and treatment regimens for the sequelae of COVID-19. While COVID-19 continues to affect many people around the world, AF may be a significant cause for morbidity and mortality.

Infection Prevention & Control

- This randomised, double-blind, placebo-controlled trial in the Unites States, Romania, and Moldova assessed the effectiveness of casirivimab and imdevimab (CAS + IMD) in preventing symptomatic SARS-CoV-2 infections over a 7-month follow-up period. The study included 1683 participants (841 assigned to CAS + IMD and 842 assigned to placebo). During the entirety of the 8-month study, CAS + IMD reduced the risk of COVID-19 by 81.2% (nominal p<0.0001) versus placebo. During the 7-month follow-up period, protection was greatest during months 2–5, with a 100% relative risk reduction in COVID-19 (nominal p<0.0001; post-hoc analysis). Efficacy waned during months 6–8 (post-hoc analysis). Seroconversion occurred in 38 (4.5%) of 841 participants in the CAS + IMD group and in 181 (21.5%) of 842 in the placebo group during the 8-month study (79.0% relative risk reduction *vs* placebo; nominal p<0.0001). Six participants in the placebo group were hospitalised due to COVID-19 versus none who received CAS + IMD. Serious treatment-emergent adverse events (including COVID-19) were reported in 24 (1.7%) of 1,439 participants receiving CAS + IMD and in 23 (1.6%) of 1428 receiving placebo. Five deaths were reported, none of which were due to COVID-19 or related to the study drugs.

Non-pharmaceutical interventions, social distancing

- None

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 19 July 2022, Pfizer and BioNTech announced they have completed a submission to the European Medicines Agency (EMA) for an Omicron-adapted bivalent COVID-19 vaccine candidate, based on the BA.1 sub-lineage, for individuals 12 years of age and older. The previously announced safety, tolerability and immunogenicity data from a Phase 2/3 trial that found a 30 µg booster dose of the Omicron-adapted bivalent vaccine candidate elicited a superior immune response against Omicron BA.1 as compared to the current COVID-19 vaccine. The bivalent vaccine candidate was well-tolerated with a favourable safety profile. The Phase 2/3 trial in 1,234 participants 56 years of age and older elicited substantially higher neutralising antibody responses against Omicron BA.1 when compared to the current COVID-19 vaccine. The geometric mean ratios (GMRs) for the monovalent 30 µg and 60 µg vaccines compared to the current COVID-19 vaccine were 2.23 (95% CI: 1.65, 3.00) and 3.15 (95% CI: 2.38, 4.16), respectively. The GMRs for the bivalent 30 µg and 60 µg vaccines compared to the

current COVID-19 vaccine were 1.56 (95% CI: 1.17, 2.08) and 1.97 (95% CI: 1.45, 2.68), respectively. The monovalent Omicron-adapted vaccine 30 µg and 60 µg achieved a lower bound 95% confidence interval for GMR of >1.5, consistent with the regulatory requirement of super superiority. Clinical trial registration #: (NCT05049226).

- On 18 July 2022, Moderna announced the Therapeutic Goods Administration (TGA) in Australia has granted provisional registration for the use of Moderna's mRNA COVID-19 vaccine, Spikevax, in a two-dose series of 25 µg per dose for active immunization to prevent COVID-19 caused by SARS-CoV-2 in children aged 6 months to 5 years. Positive interim results from the Phase 2/3 KidCOVE study showed a robust neutralising antibody response in the 6-month to 5 years of age group after a two-dose primary series of mRNA-1273, along with a favourable safety profile. The antibody titres in the pre-specified 6 month to 23 month and 2 years to 5 years of age sub-groups met the statistical criteria for similarity to the adults in the COVE study, which satisfied the primary objective of the study. Preliminary efficacy analysis on PCR-confirmed cases collected during the Omicron wave showed similar efficacy estimates against Omicron in the 6-month to 5 years of age group to those in adults after two doses of mRNA-1273. Clinical trial registration #: (NCT04796896).
- On 14 July 2022, Moderna announced that Health Canada has approved the use of Moderna's mRNA COVID-19 vaccine, Spikevax, in a two-dose series of 25 µg per dose for active immunization to prevent COVID-19 caused by SARS-CoV-2 in children aged 6 months to 5 years. Positive interim results from the Phase 2/3 KidCOVE study showed a robust neutralising antibody response in the 6-month to 5 years of age group after a two-dose primary series of mRNA-1273, along with a favourable safety profile. The antibody titres in the pre-specified 6 month to 23 month and 2 years to 5 years of age sub-groups met the statistical criteria for similarity to the adults in the COVE study, which satisfied the primary objective of the study. Preliminary efficacy analysis on PCR-confirmed cases collected during the Omicron wave showed similar efficacy estimates against Omicron in the 6-month to 5 years of age group to those in adults after two doses of mRNA-1273. Clinical trial registration #: (NCT04796896).
- On 13 July 2022, SK bioscience announced that SKYCovione COVID-19 vaccine, has shown cross-neutralising activity against Omicron variant BA.1 following booster vaccination administered ~7 months after the primary series. The results of the Phase 1/2 clinical trial, conducted with 81 healthy adults who received a booster dose of SKYCovione 7 months after the second dose of SKYCovione, showed that the neutralising antibody titres against the Omicron variant BA.1 were 25 times the titres right after the second dose, and 72 times the titres 7 months after the second dose. SKYCovione has an acceptable safety profile based on all clinical trial data available. Most of the adverse reactions that occurred after injection were mild or moderate and transient. Clinical trial registration #: (NCT05007951).
- On 13 July 2022, Novavax announced the Novavax COVID-19 Vaccine, Adjuvanted (NVX-CoV2373) has received emergency use authorization (EUA) from the U.S. Food and Drug Administration (FDA) to provide a two-dose primary series for active immunization to prevent COVID-19 in individuals 18 years of age and over. The FDA EUA based on data from the pivotal Phase 3 clinical trial, PREVENT-19, which enrolled approximately 30,000 participants aged 18 years and over in the U.S. and Mexico. In the trial, the Novavax COVID-19 Vaccine, Adjuvanted demonstrated 90.4% efficacy (95% confidence interval [CI], 83.8% to 94.3%; P<0.001) with a reassuring safety profile. Clinical trial registration #: (NCT04611802).
- On 11 July 2022, Moderna announced new clinical data on its bivalent Omicron (BA.1) booster candidate, mRNA-1273.214 that demonstrated significantly higher neutralising antibody responses against the Omicron subvariants BA.4 and BA.5 compared to the currently authorized booster (mRNA-1273) regardless of prior infection status or age. One month after administration in previously vaccinated and boosted participants, a 50 µg booster dose of mRNA-1273.214, among participants without prior infection, bivalent mRNA-1273.214 resulted in significantly higher neutralising titres against BA.4/5 compared to the currently authorized booster, with a geometric mean ratio of 1.69 (95% CI: 1.51-1.90)1. One month after booster, BA.4/5 neutralising titres were 776 (95% CI: 719, 838) for mRNA-1273.214 and 458 (95% CI: 421, 499) for the currently authorized booster. The BA.4/5 geometric mean fold rise (GMFR) from pre-booster levels was 6.3-fold (95% CI: 5.7, 6.9) for mRNA-1273.214 recipients, and 3.5-fold (95% CI: 3.2, 3.9) for mRNA-1273 recipients. Consistent results were

demonstrated across subgroups, including in those age 65 and older. Clinical trial registration #: (NCT05249829).

- On 8 July 2022, Pfizer announced the U.S. Food and Drug Administration (FDA) approved their COVID-19 vaccine, COMIRNATY (COVID-19 Vaccine, mRNA), to include individuals 12 through 15 years of age. The approval is based on data from a Phase 3 clinical trial of 2,260 participants 12 through 15 years of age. A two-dose primary series of the vaccine (30-µg dose) elicited SARS-CoV-2–neutralising antibody geometric mean titres (GMTs) of 1,239.5, demonstrating strong immunogenicity in a subset of adolescents one month after the second dose. This compared well (was non-inferior) to GMTs elicited by participants aged 16 to 25 years old (705.1 GMTs) in an earlier analysis. In the trial, a two-dose primary series of the vaccine (30-µg dose) was also 100% effective (95% confidence interval [CI, 87.5, 100.0]) in preventing COVID-19, measured between a week and more than four months after the second dose. During this time, all 30 cases of confirmed symptomatic COVID-19 were in the placebo group (n=1,109) and no cases were in the COMIRNATY group (n=1,119). No cases of severe disease occurred in either the COMIRNATY or placebo group. The adverse event profile was generally consistent with other clinical data for the vaccine, with a favourable safety profile observed across 6 months of safety follow-up data after the second dose. Clinical trial registration #: (NCT05212610).
- On 8 July 2022, Pfizer and BioNTech announced they have submitted a variation to the European Medicines Agency (EMA) requesting to update the Conditional Marketing Authorization (CMA) in the European Union (EU) with data supporting the vaccination of children ages 6 months to less than 5 years with the 3-µg dose of COMIRNATY (COVID-19 vaccine, mRNA) as a three dose series. The 3-µg dose was carefully selected as the preferred dose for children less than 5 years of age based on safety, tolerability, and immunogenicity data. The submission included data from a Phase 2/3 randomised, controlled trial that included 4,526 children 6 months to less than 5 years of age. In the trial, children received the third 3-µg dose at least two months after the second dose at a time when Omicron was the predominant variant. Following a third dose in this age group, the vaccine was found to elicit a strong immune response, with a favourable safety profile similar to placebo. No new safety signals were identified, and the frequency of adverse reactions observed in children 6 months to less than 5 years were generally lower than in children 5 to less than 12 years. Clinical trial registration #: (NCT05168709).
- On 7 July 2022, Novavax announced the submission of a request to Swissmedic to expand the conditional marketing authorization (CMA) of Nuvaxovid (NVX-CoV2373) COVID-19 vaccine in Switzerland for active immunization to prevent COVID-19 in adolescents aged 12 through 17 years and as a booster dose for individuals aged 18 and over. The request based on data from the ongoing paediatric expansion of PREVENT-19, a pivotal Phase 3 trial of 2,247 adolescents aged 12 through 17 years across 73 sites in the U.S., to evaluate the safety, effectiveness (immunogenicity), and efficacy of Nuvaxovid. In the trial, Nuvaxovid achieved its primary effectiveness endpoint and demonstrated 80% clinical efficacy overall at a time when the Delta variant was the predominant circulating SARS-CoV-2 strain in the U.S. Clinical trial registration #: (NCT04611802).

Therapeutics trials:

- On 15 July 2022, the UNC Gillings School of Global Public Health reported findings of a large randomised, placebo-controlled clinical trial led by the National Institutes of Health (NIH), with support from the Duke Clinical Research Institute (DCRI) and the UNC Gillings School of Global Public Health, which shows that treating adults hospitalised with COVID-19 with infliximab or abatacept – drugs widely used to treat certain autoimmune diseases – did not significantly shorten time to recovery but did substantially improve clinical status and reduce deaths. Some COVID-19 patients experience an immune response in which the immune system unleashes excessive amounts of proteins that trigger inflammation that can lead to acute respiratory distress syndrome, multiple organ failure, and other life-threatening complications. Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV-1) Immune Modulators clinical trial to determine if certain drugs that help minimize the effects of an overactive immune response could speed recovery and reduce deaths in adults hospitalised with moderate to severe COVID-19 was conducted. Randomly enrolled participants were assigned to one of the immune modulator drugs or placebo. Participants also received local standard of care: about

90% received remdesivir (Veklury) and about 85% received dexamethasone. The 518 participants receiving infliximab had a death rate of 10%, compared to 14.5% for the 519 participants receiving placebo, resulting in 5% lower adjusted odds of dying. Participants in the infliximab group had 43.8% better odds of clinical improvement than those in the placebo group. The 509 participants receiving abatacept had a death rate of 11%, compared to 15% for the 513 participants receiving placebo, resulting in 37.4% lower adjusted odds of dying. Participants in the abatacept group had 34.2% better odds of clinical improvement than those in the placebo group. Clinical trial registration #: (NCT04593940).

- On 12 July 2022, Humanigen, was informed of preliminary topline results from the National Institute of Allergy and Infectious Diseases' (NIAID) ACTIV-5/BET-B trial evaluating lenzilumab plus remdesivir versus placebo plus remdesivir in hospitalised COVID-19 patients. The trial did not achieve statistical significance on the primary endpoint, which was defined as the proportion of patients with baseline CRP<150 mg/L and age<85 years, alive and without mechanical ventilation through Day 29. The data also showed a non-significant trend toward a reduction in mortality in the overall patient population [HR 0.72]. There were no new safety signals attributed to lenzilumab in the ACTIV-5/BET-B study. Clinical trial registration #: (NCT04583969).
- On 8 July 2022, Moleculin reported preliminary results from the second cohort of the first-in-human Phase 1a study of WP1122. This cohort consisted of 8 subjects dosed with 16 mg/kg or placebo in the dose escalation trial evaluating the safety and pharmacokinetics (PK) of WP1122 in healthy volunteers in the United Kingdom (UK). Based on the overall results in Cohort 2, the Company deemed the cohort dose safe and well-tolerated and began its single ascending dose (SAD) Cohort 3 with a dose escalation to 32 mg/kg. The Phase 1a, first-in-human, randomised, double-blind, placebo-controlled, overlapping SAD and multiple ascending dose (MAD) is investigating the effects of WP1122 administered as an oral solution in healthy human volunteers. It is the first step in a planned investigation of WP1122 for the treatment of COVID-19. Dose escalation will take place in sequential SAD cohorts, and MAD will start as soon as SAD has successfully completed at least 3 dosing cohorts. WP1122 is recently received IND clearance from the U.S. Food and Drug Administration (FDA) to initiate a Phase 1 study of WP1122 for the treatment of Glioblastoma Multiforme (GBM). It is a metabolism/glycosylation inhibitor, a pro-drug of a well-known glucose decoy called 2-deoxy-D-glucose (2-DG). WP1122 was developed as a 2-DG prodrug to provide a more favourable pharmacological profile and was found to have greater potency than 2-DG alone in preclinical models where tumour cells require higher glycolytic activity than normal cells. WP1122 has also been shown to have a greater antiviral effect than 2-DG against SARS-CoV-2 in MRC-5 cells in culture. Clinical trial registration #: (NCT05365321).
- On 8 July 2022, MGC Pharmaceuticals obtained study and importation approval from the South African Health Products Regulatory Authority to conduct the Phase IIb dose-finding clinical trial of CimetrA in Covid-19 patients. A nanoparticle micellar formulation, CimetrA is based on the pharmaceutical synergetic composition comprising Curcumin and Boswellia. In a double-blind, placebo-controlled Phase 2 trial, CimetrA demonstrated immunomodulatory and anti-inflammatory effects in moderate Covid-19 patients. The phase 2b trial in South Africa is an expansion of the dosing trial presently progressing in a site at Rambam Medical Center, Haifa and Israel. It will incorporate key parameters, including detecting the most effective dose of CimetrA, a complete safety and Pharmacovigilance profile and an extensive Pharmacokinetic profile of the drug. In addition, the anti-inflammatory and immune-modulatory effects of CimetrA via Cytokine level monitoring will be evaluated in the trial.
- On 6 July 2022, the U.S. Food and Drug Administration revised the Emergency Use Authorization (EUA) for Paxlovid (nirmatrelvir and ritonavir), to authorize state-licensed pharmacists to prescribe Paxlovid to eligible patients, with certain limitations to ensure appropriate patient assessment and prescribing of Paxlovid. Paxlovid is authorized for the treatment of mild-to-moderate COVID-19 in adults and paediatric patients (12 years of age and older weighing at least 40 kilograms or about 88 pounds) with positive results of direct SARS-CoV-2 viral testing, who are at high risk for progression to severe COVID-19, including hospitalisation or death. Patients in the authorized population who report a positive home test result from a rapid antigen diagnostic test, or a positive PCR test, to their provider

are eligible for Paxlovid under the EUA. Confirmation of a positive home rapid antigen diagnostic test with additional direct SARS-CoV-2 viral testing, such as a PCR, is not required.

Immunotherapies trials:

- On 7 July 2022, Brii Biosciences announced the commercial launch of the amubarvimab/ romlusevimab combination, a long-acting COVID-19 neutralising antibody therapy, in China. The amubarvimab/romlusevimab combination was approved by China's National Medical Products Administration (NMPA) for the treatment of adults and paediatric patients (age 12-17 weighing at least 40 kg) with mild and normal type of COVID-19 at high risk for progression to severe disease, including hospitalisation or death. The indication of paediatric patients (age 12-17 weighing at least 40 kg) is under a conditional approval. Amubarvimab and Romlusevimab are non-competing SARS-CoV-2 monoclonal neutralising antibodies derived from convalesced COVID-19 patients. Based on the final results from ACTIV-2 Phase 3 clinical trial with 837 enrolled outpatients, the amubarvimab/romlusevimab combination demonstrates a statistically significant 80% reduction of hospitalisation and death with fewer deaths through 28 days in the treatment arm (0) relative to placebo (9), and improved safety outcome over placebo in non-hospitalised COVID-19 patients at high risk of clinical progression to severe disease. Similar efficacy rates were observed in participants initiating therapy early (0-5 days) and late (6-10 days), following symptom onset, providing critically needed clinical evidence in COVID-19 patients who were late for treatment. The live virus testing data as well as pseudovirus testing data from multiple independent labs have demonstrated that the amubarvimab/romlusevimab combination retains activity against major SARS-CoV-2 variants of concern, including the following commonly identified variants, B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), B.1.429 (Epsilon), B.1.617.2 (Delta), AY.4.2 (Delta Plus), C.37 (Lambda), B.1.621 (Mu), B.1.1.529-BA.1 (Omicron), and BA.1.1 and BA.2 (Omicron subvariants). Additional testing including live virus assays are being conducted to confirm the neutralising activity against BA.4/5 and BA.2.12.1. Clinical trial registration #: (NCT04518410).

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