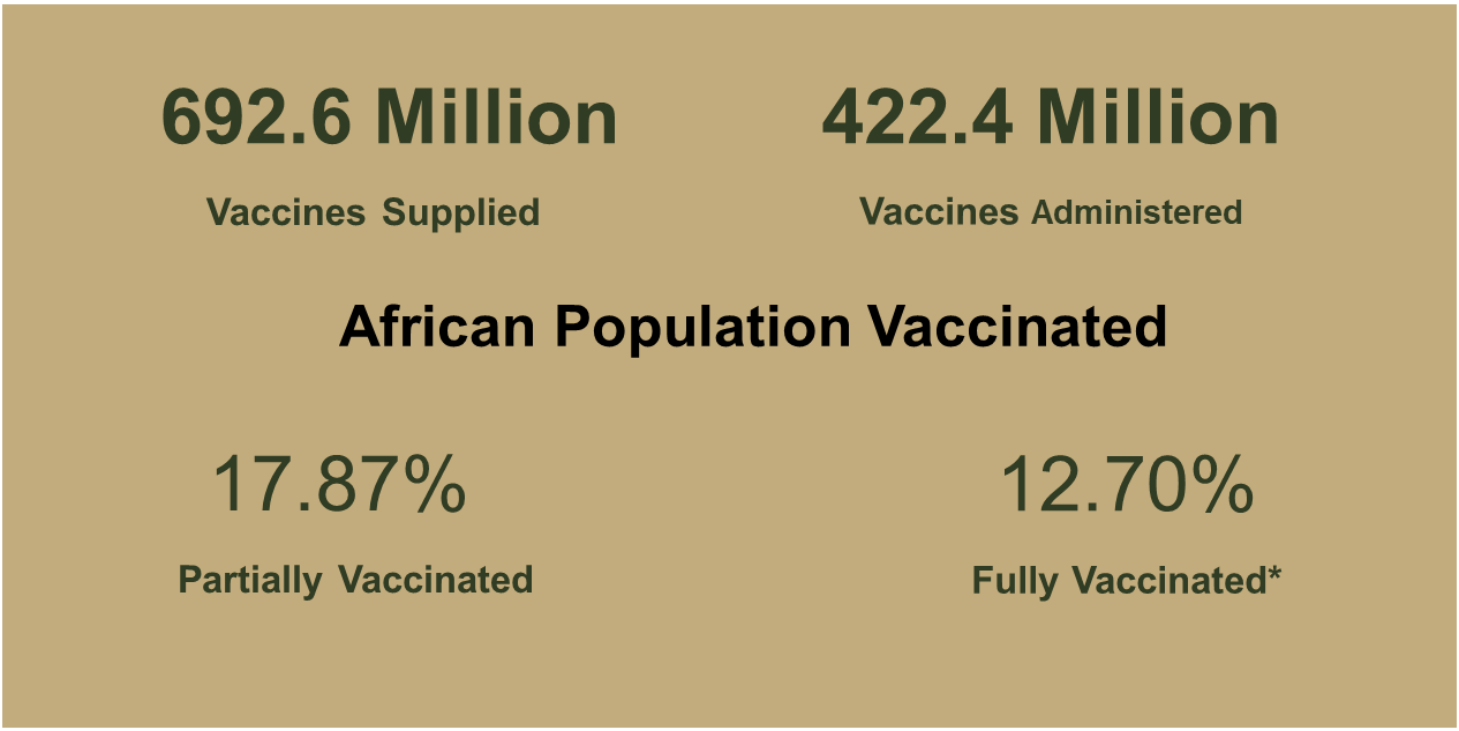
COVID-19 Scientific and Public Health Policy Update[1]

(2 March 2022)

In addition to the Weekly Outbreak Brief and other documents on the spread of COVID-19 and the actions that the African Union/Africa CDC and WHO/AFRO are taking to help African Union Member States, this biweekly brief details the latest developments in scientific knowledge and public health policy from around the world as well as updates to the COVID-19-related guidance from Africa CDC, WHO and other public health agencies. Contents of this brief are ***not intended to serve as recommendations*** *from the African Union-Africa CDC or WHO/AFRO; rather, the brief serves as a summary of the scientific information available in the public space to Member States. It is important to note that the outbreak is evolving rapidly and that the nature of this information will continue to change. We will provide regular updates to ensure Member States are informed of the most critical developments on the science and public health best practices related to COVID-19.*

A. Trending Topics

Status of Vaccines in Africa

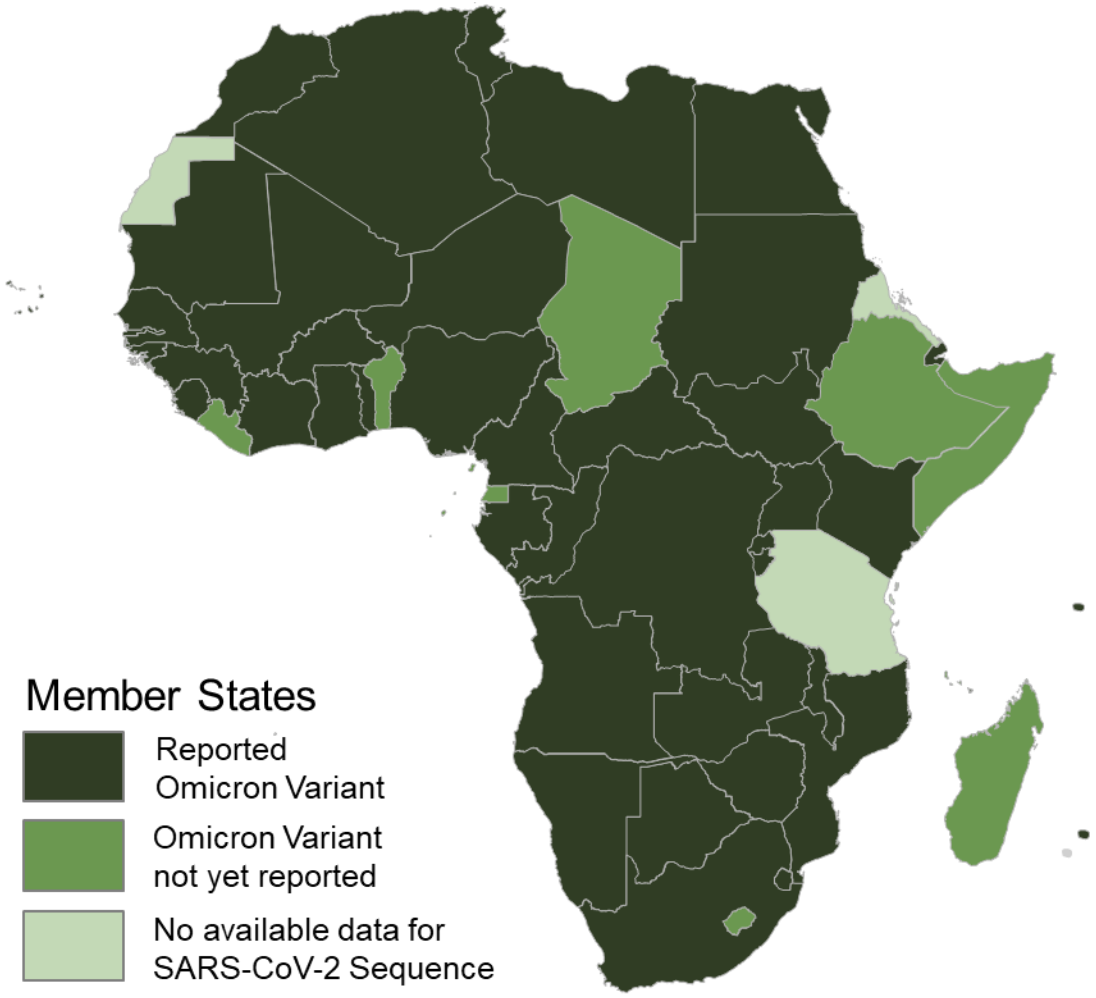


*Received two doses of a two dose COVID-19 vaccine series or one dose of the Johnson & Johnson vaccine
https://africacdc.org/COVID-19-vaccination/
Updated 2nd March, 2022

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

Variants of Concern

- The Omicron variant (B.1.1.529), first reported in South Africa on 24th November 2021, has spread to 182 countries worldwide. As of 2 March 2022, 42 (76.4%) of the 55 Member States in Africa have reported this variant. https://africacdc.org/institutes/africa-pathogen-genomics-initiative/



Updated 2nd March, 2022

B. New guidelines and resources

Since 15th February 2022,

- Africa CDC[2] has published new guidance and resources on:
  - Partnerships for African Vaccine Manufacturing (PAVM) Framework for Action
  - Interim guidance on COVID-19 Rapid Antigen self-testing to African Union Member States
  - Africa CDC – Mastercard Foundation: Saving Lives and Livelihoods Newsletter, February 2022

- U.S. CDC[3] has published new guidance and resources on:
  - Interim Guidance on Developing a COVID-19 Case Investigation & Contact Tracing Plan: Overview
  - Prioritizing Case Investigations and Contact Tracing for COVID-19 in High Burden Jurisdictions
  - Using Antibody Tests for COVID-19

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

- WHO[4] has published new guidance and resources on:
  - Therapeutics and COVID-19: living guideline
  - Mental Health and COVID-19: Early evidence of the pandemic's impact: Scientific brief
  - Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19
  - Annexes to the recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19
  - Contact tracing and quarantine in the context of the Omicron SARS-CoV-2 variant: interim guidance

- U.S. FDA[5] has issued press releases on:
  - On 1st March, the FDA issued a safety communication warning people not to use the ACON Laboratories "Flowflex SARS-CoV-2 Antigen Rapid Test (Self-Testing)."
  - On 1st March, the FDA issued a safety communication warning people not to use the SD Biosensor STANDARD Q COVID-19 Ag Home Test
  - On 24th February, the FDA revised the emergency use authorization for Evusheld (tixagevimab co-packaged with cilgavimab) to change the dosing for the authorized use as pre-exposure prophylaxis
  - On 24th February, the FDA updated the Antibody (Serology) Testing for COVID-19: Information for Patients and Consumers page
  - As of 1st March, 420 tests and sample collection devices are authorised by the FDA under emergency use authorisations

- ECDC[6] has issued new resources on:
  - Data collection on COVID-19 outbreaks in closed settings: long-term care facilities, version 2.1

- UKHSA[7] has issued new guidance and press releases on:
  - COVID-19 test validation approved products
  - COVID-19 vaccinations received overseas
  - COVID-19: guidance on protecting people defined on medical grounds as extremely vulnerable
  - COVID-19: workplace testing terms and conditions
  - SARS-CoV-2 variants of public health interest: 25 February 2022
  - Monitoring reports of the effectiveness of COVID-19 vaccination
  - COVID-19 serology and viral detection tests: technical validation reports

Scientific updates

Basic Science

- This case-control study in Japan examined the expression of SARS-CoV-2 nucleocapsid protein and angiotensin-converting enzyme 2 (ACE2) in lacrimal gland tissues of a patient with COVID-19 and a patient without COVID-19. Both patients were Japanese women aged 35 years (case) and 43 years (control). The case had lacrimal gland enlargement for 6 months. Histopathologic analysis of surgically excised lacrimal gland tissues from the patient with COVID-19 showed characteristic glandular damage and polymorphonuclear leukocyte infiltration within the epithelium, together with marked inflammation made up of lymphocytes and plasma cells surrounding the glands. Immunoreactivity for nucleocapsid protein of SARS-CoV-2 as well as angiotensin-converting enzyme 2 was noted in the lacrimal gland

[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

tissue. Their findings suggest that SARS-CoV-2 may target lacrimal gland tissue and manifest as chronic inflammation.

- This descriptive study in Laos highlighted the diversity of bat coronaviruses and identified the sequences that contribute to the virus' mosaicism. The authors performed complete genomic sequencing of faecal samples from 645 bats belonging to 6 families and 46 species. They found that sarbecoviruses circulate in cave bats living in the limestone karstic terrain in northern Laos, near the southern border of China. Receptor binding domains (RBDs) of the viruses differ from that of SARS-CoV-2 by only one or two residues at the interface with cellular angiotensin-converting enzyme 2 (ACE2) and bind more efficiently to the human ACE2 protein than the SARS-CoV-2 Wuhan strain isolated in early human cases. They also mediate hACE2-dependent entry and replication in human cells, which is inhibited by antibodies neutralising SARS-CoV-2. None of the identified bat viruses harboured a furin cleavage site in the spike. Their findings indicate that bat-borne SARS-CoV-2-like viruses potentially infectious to humans circulate in *Rhinolophus* spp. in northern Laos.
- This cohort study in Italy investigated a population of 1873 health care workers (HCWs) who were recipients of the BNT162b2 vaccine. Of the study population, 1584 were immunologically naïve to SARS-CoV-2 (IN) and 289 had a history of previous infection (PI). The authors performed analyses of the humoral response (IgG and IgM antibodies specific for the SARS-CoV-2 spike protein, IgG-S and IgM-S) in samples collected before administration (T0), at the second dose (T1) and 3 weeks after the second dose (T2). They observed three unconventional patterns of antibody response in naïve vaccinees: 1) initial absence of detectable IgM, 2) development of IgM following IgG appearance, and 3) simultaneous presence of IgM and IgG. Among the three, the latter was associated with a more efficient response in both anti-SARS-CoV-2 IgG-S levels and virus-neutralising activity, following vaccination.

Vaccines

- This cohort study in Hong Kong examined the rates of myocarditis-related hospitalisations following receipt of 2 doses compared to 1 dose of BNT162b2 vaccination in adolescents. Since 15th September 2021, adolescents (aged 12-17 years) in Hong Kong have been recommended to receive 1 dose of BNT162b2 instead of 2 doses 21 days apart. A total of 224,560 first doses and 162,518 second doses of BNT162b2 vaccine was administered to adolescents. Forty-three adolescents had myocarditis-related hospitalisation following receipt of BNT162b2 vaccination, and 84% of these hospitalisations (36 of 43) occurred following receipt of the second dose. The incidence rate of myocarditis was 3.12 (95% CI, 1.25-6.42) and 22.15 (95% CI, 15.51-30.67) per 100 000 persons for the first and second dose, respectively. The cumulative incidence of myocarditis decreased from 43 cases in 202,315 adolescents vaccinated (21.25, 95% CI, 15.38-28.63) per 100 000 persons to 0 cases in 22,245 adolescents vaccinated following implementation of the single-dose policy. The findings suggest that the single-dose regimen was associated with reduction in myocarditis risk among vaccinated adolescents.
- This cohort study in Israel assessed the association between the BNT162b2 mRNA COVID-19 vaccine and sudden sensorineural hearing loss (SSNHL). Of 2,602,557 individuals who received the first dose of the BNT162b2 vaccine, 91 developed SSNHL. Of the initial study population, 2,441,719 (93.8%) received the second dose, of whom, 79 developed SSNHL. The age- and sex-weighted standardized incidence ratios (SIRs) were 1.35 (95% CI, 1.09-1.65) after the first vaccine dose and 1.23 (95% CI, 0.98-1.53) after the second vaccine dose. After the first vaccine dose, the estimated SIRs were more pronounced in female patients aged 16 to 44 years (SIR, 1.92; 95% CI, 0.98-3.43) and female patients 65 years or older (SIR, 1.68; 95% CI, 1.15-2.37). After the second vaccine dose, the highest SIR was observed in male patients 16 to 44 years (SIR, 2.45; 95% CI, 1.36-4.07). The attributable risks were generally small, and the results were similar when 2019 was used as a reference to estimate the expected number of SSNHL cases. Their findings suggest that the BNT162b2 vaccine might be associated with increased risk of SSNHL; however, the effect size is very small.
- This systematic review and meta-analysis of 22 studies assessed the risk of severe immediate allergic reactions (e.g., anaphylaxis) to a second dose of SARS-CoV-2 mRNA vaccine among persons with immediate allergic reactions to their first vaccine dose. The authors found that, among 1366 patients

revaccinated under the supervision of an allergist, there was a low incidence (0.16%) of immediate severe allergic reactions associated with receiving a second dose of SARS-CoV-2 mRNA vaccine. There were no deaths. These findings suggest that revaccination of individuals with an immediate allergic reaction to a first SARS-CoV-2 mRNA vaccine dose can safely receive a second dose in a supervised setting equipped to manage severe allergic reactions.

- This multicentre, prospective cohort study among 35,768 asymptomatic health care workers in the United Kingdom assessed the durability of protection against SARS-CoV-2 infection conferred by both infection-acquired and vaccine-acquired immunity. The authors found that BNT162b2 vaccine administered with a short or long interval between two doses was associated with a considerably reduced risk of SARS-CoV-2 infection (asymptomatic and symptomatic) in the short term, but this protection waned after 6 months, during a period when the delta variant was predominant. Infection-acquired immunity boosted with vaccination remained high more than 1 year after infection. These findings have implications in the strategic use of booster doses of vaccines to avert waning of protection against infection and transmission of SARS-CoV-2.
- This test negative case-control study estimated vaccine effectiveness against symptomatic COVID-19 caused by the omicron variant in persons 18 years of age or older in England. Vaccine effectiveness was calculated following primary immunization with two doses of BNT162b2, ChAdOx1 nCoV-19, or mRNA-1273 vaccine and after receipt of a booster dose of BNT162b2, ChAdOx1 nCoV-19, or mRNA-1273. The authors found that primary immunization with two doses of ChAdOx1 nCoV-19 or BNT162b2 vaccine provided limited protection against symptomatic disease caused by the omicron variant. A BNT162b2 or mRNA-1273 booster following either the ChAdOx1 nCoV-19 or BNT162b2 primary course substantially increased protection, but that protection waned over time.
- This case series study conducted in the United States (US) describes 21 individuals with illness meeting the US CDC's multisystem inflammatory syndrome in children (MIS-C) case definition. The study utilised surveillance results from the first 9 months of the COVID-19 vaccination programme in the US. The findings suggest that MIS-C is rare among COVID-19 vaccine recipients without evidence of a prior SARS-CoV-2 infection (reporting rate < 1 case per million vaccinated individuals aged 12–20 years). The authors emphasised the importance of continued surveillance for MIS-C illness following COVID-19 vaccination, especially as paediatric COVID-19 vaccination is authorised for younger children. The majority of MIS-C cases following SARS-CoV-2 infection are less than 20 years of age.

Diagnostics

- This study in Israel presents a ready-to-use breath analysis method for SARS-CoV-2 screening that utilises Fourier-transform infrared (FTIR) spectroscopy combined with an artificial intelligence (AI) generated algorithm applied to FTIR result interpretation. The entire process is performed by a mobile point-of-care machine within less than 3 minutes. The study focuses on using a disease specific spectrometric profile for SARS-CoV-2 diagnosis rather than the identification of disease specific molecules. The study also presents two phases of validation data obtained through expert determination of SARS-CoV-2 status based on AI algorithm generated criteria. In both phases, the AI algorithm results indicated a 1:1 correlation with the “gold standard” PCR. This device is the first to offer a practical solution for rapid, non-invasive SARS-CoV-2 screening in settings such as airports and sports arenas.
- This study in the United Kingdom investigated 1) the proportion of lateral flow tests (LFTs) that produce negative results in those with a high risk of infectiousness from SARS-CoV-2, 2) the impact of the stage and severity of disease, and 3) compared findings with predictions made by influential mathematical models. Their analysis predicted that of those with a viral culture positive result, Innova would miss 20% attending an NHS Test-and-Trace centre, 29% without symptoms attending municipal mass testing, and 81% attending university screen testing without symptoms, along with 38%, 47%, and 90% of sources of secondary cases. The proportion of infectious people with SARS-CoV-2 missed by LFTs is substantial enough to be of clinical importance. Results from key models have substantially overestimated the sensitivity of LFTs compared with empirical data.
- This study conducted in Canada presents findings from a workplace frequent rapid antigen test (RAT) program. The screening program was able to identify 473 asymptomatic individuals who tested positive

on the RAT and confirmed positive by a nasopharyngeal polymerase chain reaction (PCR) diagnostic test. Of the 4300 RATs performed, one worker (< 0.2%) was presumptive positive, but later tested PCR negative. False positives did not meaningfully disrupt workplace operations. Most employers rated the program highly and expressed that the program greatly contributed to workplace and community safety. Their findings describe a sustained and scalable implementation plan for establishing a frequent workplace testing program.

Care and Treatment

- This randomised, double-blind, placebo-controlled trial across 36 centres in the United States found that treatment of outpatients with mild or moderate COVID-19 with nitazoxanide 300 mg extended-release tablets administered orally 600 mg twice daily for five days may reduce the risk of progression to severe illness in participants at high risk and the time to sustained recovery in patients with mild illness. The trial enrolled 1092 participants. Larger trials are being undertaken to confirm initial results.

Epidemiology

- This prospective study in South Africa assessed the disease severity following infection with the Omicron sub-lineages BA.2 and BA.1. The authors used individual patient level data linked from three different national health data sources for the period of 1 December, 2021 to 20 January, 2022. The proportion of S-gene positive infections (BA.2 proxy) increased from 3% (931/31,271) to 80% (2,425/3,031) during this study period. The odds of hospitalisation were similar between individuals with S-gene positive infection compared to S-gene Target Failure (BA.1 proxy) infection (aOR 0.96, 95%CI 0.85-1.09). Moreover, among hospitalised individuals, after controlling for factors associated with severe disease, the odds of severe disease did not differ for individuals with S-gene positive infection compared to SGTF infection (aOR 0.91, 95%CI 0.68-1.22). Their findings suggest that while BA.2 may have a competitive advantage over BA.1 in some settings, the clinical profile of illness remains similar. [*not peer reviewed*]
- This study utilised spatial analyses to show that the earliest known COVID-19 cases diagnosed in December 2019 were geographically located near to, or centred on, the Huanan Seafood Wholesale Market. By combining spatial and genomic data, the authors show that the two early lineages of SARS-CoV-2 have a clear association with the Huanan market. They also report that live mammals, including raccoon dogs, were sold at the market in late 2019 and geospatial analyses within the market show that SARS-CoV-2-positive environmental samples were strongly associated with vendors selling live animals. Together, their analyses provide dispositive evidence for the emergence of SARS-CoV-2 via the live wildlife trade and identify the Huanan market as the unambiguous epicentre of the COVID-19 pandemic. [*not peer reviewed*]
- This cross-sectional study estimated the seroprevalence of SARS-CoV-2 IgG in Gauteng, South Africa from 22 October to 9 December 2021. The authors obtained samples from 7010 participants, of whom 1319 (18.8%) had received a COVID-19 vaccine. The seroprevalence of SARS-CoV-2 IgG ranged from 56.2% (95% CI, 52.6 to 59.7) among children younger than 12 years of age to 79.7% (95% CI, 77.6 to 81.5) among adults older than 50 years of age. Vaccinated participants were more likely to be seropositive for SARS-CoV-2 than unvaccinated participants (93.1% vs. 68.4%). Epidemiologic data showed that the incidence of SARS-CoV-2 infection increased and subsequently declined more rapidly during the fourth wave than it had during the three previous waves. The incidence of infection was decoupled from the incidences of hospitalisation, recorded death, and excess death during the fourth wave, as compared with the proportions seen during previous waves.
- This cohort study in the United States characterises transmission and infection of SARS-CoV-2 among vaccinated and unvaccinated attendees of an indoor wedding reception. The study was conducted in July 2021 among 75 individuals, of whom 56 (75%) were fully vaccinated, 4 (5%) were partially vaccinated, and 15 (20%) were unvaccinated. The authors found that nearly half (47%) of attendees at the reception who were tested were infected with the Delta variant of SARS-CoV-2. Unvaccinated attendees had a higher risk of SARS-CoV-2 infection than vaccinated attendees (risk ratio, 2.64; 95% CI, 1.71-4.06; $P = .001$), secondary transmission from vaccinated attendees to vaccinated and unvaccinated contacts (outside of the reception) was observed, and the index case was identified as

an unvaccinated symptomatic child. These findings suggest that unvaccinated people are at increased risk of contracting SARS-CoV-2 compared with vaccinated people in large social gatherings.

- This systematic review evaluated the comparable proportion of participants recruited in randomised clinical trials (RCTs) for COVID-19 from low- and middle-income (LMIC) countries and high-income countries (HIC) (using World Bank definitions) relative to disease burden in the respective regions. The authors also examined these proportions stratified by COVID-19 vaccine and nonvaccine RCTs. They found that there were 295 845 participants in 71 RCTs (75% nonvaccine and 25% vaccine), of which 247 631 (84%) were recruited in HIC-sponsored RCTs and 48 214 (16%) in LMIC-sponsored RCTs. Forty-nine RCTs (69%) had a HIC sponsor. Their findings show that COVID-19 has amplified inequalities in global health and socioeconomic outcomes between HICs and LMICs. They recommend strengthening research capacity in LMICs, mobilizing funding from diverse sources, identifying relevant translatable research priorities, and establishing research partnerships to mitigate the effect of inequalities on COVID-19 outcomes in LMICs.
- This retrospective cohort study in the United States evaluated the association of SARS-CoV-2 infection with serious maternal morbidity or mortality from common obstetric complications. The study included 14,104 patients from 17 hospitals. The authors found that a composite outcome of maternal death or serious morbidity related to hypertensive disorders of pregnancy, postpartum haemorrhage, or infection other than SARS-CoV-2 occurred significantly more frequently in individuals with SARS-CoV-2 infection compared with individuals without SARS-CoV-2 infection (13.4% vs 9.2%; difference, 4.2% [95% CI, 2.8%-5.6%]; adjusted relative risk [aRR], 1.41 [95% CI, 1.23-1.61]).
- This prospective cohort study in 23 intensive care units (ICUs) in France examined the association between patient hospitalisation for COVID-19 acute respiratory distress syndrome (ARDS) versus ARDS from other causes and the risk of posttraumatic stress disorder (PTSD)–related symptoms in family members. Among 517 family members of ICU patients, PTSD-related symptoms at 90 days after ICU discharge were significantly more common in family members of patients with COVID-19 ARDS compared with non–COVID-19 ARDS (35% vs 19%). In a multivariable analysis adjusting for age, sex, and level of social support, COVID-19 ARDS was independently associated with PTSD-related symptoms in family members (odds ratio, 2.05 [95% CI, 1.30 to 3.23]). They recommend for interventions to improve well-being after traumatic events.
- This study reports on the analysis of the German Registry of COVID-19 Autopsies database. The database included 1129 COVID-19 autopsy cases from 29 autopsy centres. The authors analysed 1095 eligible cases with positive clinical or post-mortem SARS-CoV-2 test to describe the autopsy rate per calendar week, patient demographics (i.e., sex and age), disease duration, SARS-CoV-2 RNA detection at autopsy, and cause of death. The chain of events analysis identified COVID-19 as the underlying cause of death in 86% of the autopsy cases. In the remaining 14%, COVID-19 was a concomitant infection. The most common immediate cause of death was diffuse alveolar damage, followed by multi-organ failure. The authors also presented insight on the benefits of analysing data from central autopsy registries. For example, such an analysis can provide information from decentralized archived biomaterial, and the use of these material for generating results to inform public health decision makers.

Infection prevention & control

- This cross-sectional study in 81 countries across all six WHO regions and income levels assessed the implementation of infection prevention and control (IPC) programs in health facilities. A total of 4440 IPC professionals completed the online WHO IPC assessment framework (IPCAF) between 16th January to 31st December 2019. The overall weighted IPCAF median score indicated an advanced level of implementation (605, IQR 450.4–705.0), but significantly lower scores were found in low-income (385, 279.7–442.9) and lower-middle-income countries (500.4, 345.0–657.5), and public facilities (515, 385–637.8). Core component 8 (built environment) and core component 2 (guidelines) scored the highest, and core component 7 (workload, staffing, and bed occupancy) and core component 3 (education and training) scored the lowest. Overall, only 15.2% of facilities met all IPCAF minimum requirements, ranging from 0% in low-income countries to 25.6% in primary facilities, 9% in secondary facilities, and 19% in tertiary facilities in high-income countries. There exist important gaps

in IPC facility implementation and core components across income levels that hinder IPC progress. They recommend increased support for more effective and sustainable IPC programs to reduce risks posed by outbreaks to global health security and to ensure patient and health worker safety.

- This cross-sectional study in 90 countries assessed the level of hand hygiene implementation and its drivers in health-care facilities. A total of 3206 IPC professionals completed the online WHO Hand Hygiene Self-Assessment Framework (HHSAF) survey between 16th January to 31st December 2019. The HHSAF survey score for hand hygiene implementation indicated an intermediate level across the 90 countries (350 points, IQR 248–430). This score was positively associated with country income level and health-care facility funding structure. Overall, highest score was observed for System Change (85 points, IQR 55–100). This reflects the use of alcohol-based hand rub at the point of care at standard practice in many health-care facilities, especially in high-income countries. The lowest score was observed for Institutional Safety Climate (55 points, IQR 35–75). From 2015 to 2019, the median HHSAF score in health-care facilities participating in both HHSAF surveys (n=190) stagnated. Availability of resources, leadership, and organisational support are key elements to further improve quality of care and provide access to safe care for all.

Non-pharmaceutical interventions, social distancing

- This systematic review on contact tracing considers evidence of disease control effectiveness across multiple infectious diseases (COVID-19, tuberculosis, HIV, curable sexually transmitted infections, and measles). More than 2 million index patients were included from 47 studies across a variety of settings (both urban and rural areas and low-resource and high-resource settings). Forty (40) studies compared provider-initiated contact tracing with other interventions or evaluated expansions of provider-initiated contact tracing, and 7 compared programmatic adaptations within provider-initiated contact tracing. Twenty-nine (72.5%) of the 40 studies evaluating the effect of provider-initiated contact tracing, including 4 of 6 COVID-19 studies, found contact tracing interventions were associated with improvements in case detection, decreased secondary transmission, and lower overall disease incidence. However, the use of diverse approaches and reliance on observational designs limited the authors' ability to describe the most effective use of contact tracing as the primary means for disease control.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 28th February 2022, Novavax shared extended analysis results of its Phase 3 clinical trial of the protein-based COVID-19 vaccine, NVX-CoV2373 conducted in the United Kingdom (UK). NVX-CoV2373 is a protein-based vaccine engineered from the genetic sequence of the first strain of SARS-CoV-2 that can neither replicate, nor cause COVID-19. High level of vaccine efficacy was maintained over a 6-month period surveillance. The analysis showed vaccine efficacy of 82.5% (95% CI: 75.0, 87.7) in protection against all COVID-19 infections – both symptomatic and asymptomatic and 100% (95% CI: 17.9, 100) against severe disease – as measured by PCR+ or anti-N seroconversion. The vaccine showed a reassuring safety profile with adverse events balanced between vaccine and placebo groups. Clinical trial registration #: (NCT04583995).
- On 24th February 2022, Pfizer and BioNTech announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion on the administration of the COVID-19 vaccine COMIRNATY as a booster dose (30ug) at least six months after the second dose in adolescents 12 through 17 years of age. The opinion based on analysis of interim safety and efficacy data from a clinical trial of a vaccine booster dose among those aged 16 and over, published literature, post authorisation data and real-world evidence from the use of booster doses in young patients in Israel.
- On 24th February 2022, Medicago and GlaxoSmithKline (GSK) announced the approval by Health Canada of COVIFENZ, an adjuvanted plant-based virus-like particles recombinant COVID-19 vaccine. The vaccine is indicated for active immunization to prevent COVID 19 in individuals 18 to 64 years of

age. COVIFENZ uses Coronavirus-Like Particle (CoVLP) technology with the vaccine composed of recombinant spike (S) glycoprotein expressed as virus-like particles (VLPs) co-administered with GSK's pandemic adjuvant. The vaccination regimen calls for two doses given intramuscularly 21 days apart (3.75 micrograms of CoVLP antigen in combination with GSK pandemic adjuvant in the same injection). Clinical trial registration #: (NCT05040789).

- On 24th February 2022, Moderna announced the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending a variation to the conditional marketing authorization (CMA) to include a 50 µg two-dose series of Spikevax vaccine against COVID-19, in children ages 6-11 years. This was based on the ongoing Phase 2/3 "KidCOVE" study, a randomised, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of Spikevax (mRNA-1273) given to healthy children 28 days apart. Data submitted to the CHMP from over 4,000 children demonstrated that vaccination of children ages 6-11 years with a 50 µg mRNA-1273 primary series is associated with non-inferior anti-SARS-CoV-2 neutralising antibody responses when compared to individuals 18-25 years old from the Phase 3 COVE study. Positive direct efficacy of two 50 µg doses of mRNA-1273 was also demonstrated and vaccination was generally well tolerated. Clinical trial registration #: (NCT04796896).
- On 23rd February 2022, Sanofi and GlaxoSmithKline (GSK) announced their intent to submit data from both their booster and Phase 3 efficacy trials as the basis for regulatory applications for a COVID-19 vaccine. The public health relevance of the refrigerator temperature-stable adjuvanted protein-based Sanofi-GSK vaccine is strongly supported by the induction of robust immune responses and a favourable safety profile in multiple settings. Final analysis of the global VAT02 booster trial confirms universal ability to boost neutralising antibodies 18- to 30-fold across vaccine platforms (mRNA, adenovirus). In the VAT08 Phase 3 primary series trial, two doses of the Sanofi-GSK vaccine in seronegative populations demonstrated 100% efficacy against severe COVID-19 disease and hospitalisations; 75% efficacy against moderate or severe COVID-19 disease and 57.9% efficacy against any symptomatic COVID-19 disease. Clinical trial registration #: (NCT04904549).
- On 16th February 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 50 µg dose, two-dose series, for active immunization to prevent COVID-19 caused by SARS-CoV-2 in children aged 6-11 years. This was based on the submitted results of a Phase 2 "KidCOVE" study, a randomised, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of two 50 µg doses of Spikevax (mRNA-1273) given to healthy children 28 days apart. The study population was divided into three age groups (6 to under 12 years, 2 to under 6 years, and six months to under 2 years). Data submitted from the Phase 3 Cove study demonstrated that vaccination of children 6 to under 12 years of age with a 50 µg mRNA-1273 primary series is associated with non-inferior anti-SARS-CoV-2 neutralising antibody responses when compared to that in individuals 18-25 years old. The geometric mean ratio (GMR) comparing the response in children to the response in young adults from the Phase 3 COVE study was 1.5 (95% CI: 1.3, 1.8), with a seroresponse rate of 99.3%. Two 50 µg doses of mRNA-1273 were generally well tolerated. Clinical trial registration #: (NCT04796896).

Therapeutics trials:

- On 1st March 2022, RedHill announced positive top-line results from the Phase 2 part of the Phase 2/3 study of once-daily oral RHB-107 (upamostat) in non-hospitalised symptomatic COVID-19 patients, predominantly conducted in the U.S. (60/61 patients) as well as South Africa. RHB-107 is a proprietary, first-in-class, orally-administered antiviral, that targets human serine proteases involved in preparing the spike protein for viral entry into target cells. The results indicated a strong inhibition of SARS-CoV-2 viral replication in an in vitro human bronchial epithelial cell model. Various studies demonstrated a strong clinical safety and biodistribution profile of RHB-107. The Phase 2/3 multicentre, randomised, double-blind, placebo-controlled, parallel-group study revealed highly promising efficacy results delivering a 100% reduction in hospitalisation due to COVID-19. None of the patients receiving RHB-107 were hospitalised with COVID-19 (0/41) compared to 15% on the placebo-controlled arm requiring

hospitalisation (3/20) (nominal p-value=0.0317). Furthermore, a reduction of 87.8% in reported new severe COVID-19 symptoms was reported, with only one patient on RHB-107 (2.4%, 1/41) compared to 20% (4/20) of patients on the placebo-controlled arm experiencing new COVID-19 related severe symptoms (nominal p-value=0.036). Clinical trial registration #: (NCT04723527).

- On 28th February 2022, Virios announced a collaboration with the Bateman Horne Centre ("BHC") to explore the role of combination antiviral therapy in Long COVID which is also known as Post-Acute Sequelae of COVID-19. Long COVID impacts up to 30% of COVID-19 patients. Activation of dormant Herpes Virus infections are hypothesised as a potential trigger of Long COVID symptoms. The study will assess the therapeutic potential of IMC-2 to ease the burden of long COVID. IMC-2 is a new combination of valacyclovir and celecoxib with specific and synergistic mechanisms of action, deliberately chosen to hinder activation and replication of the herpes virus. The treatment aids in retaining the herpes viruses in a latent state or 'down-regulates' viruses from a lytic to latent state. Valacyclovir component hinders viral deoxyribonucleic acid (DNA) polymerase needed for replication. Celecoxib component hinders COX-2 and COX-1 enzymes, that are utilised by herpes viruses to expedite their replication.
- On 22nd February 2022, Skymount Medical announced approval from the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) to conduct a human clinical trial of a novel oral therapeutic for patients with mild to moderate COVID-19. The two drugs combination is designed to address both the viral load and the inflammatory aspects of COVID-19. The treatment has shown up to 97% efficacious in reducing the amount of SARS-CoV-2 in vitro and animal studies, without negative side effects. It was discovered using the DeepDrug artificial intelligence (AI) platform and is comprised of United States Food and Drug Administration (FDA) approved cancer medication and anti-parasitic agent. The DeepDrug AI platform was trained to recognize similarities between existing drugs and antiviral peptides, which target coronaviruses, and was then tested on unseen pairs where it achieved an accuracy of 97.28%—unrelated to the efficacy of the drugs themselves. The study will be a double-blind intervention comparing a two-drug combination and a single antiviral drug to a placebo. Findings will help determine the impact these therapies on the length and severity of COVID-19 symptoms.
- On 21st February 2022, UVA Health announced to joined a nationwide study evaluating two repurposed medications in the search for effective, safe treatments for mild-to-moderate COVID-19. The two medications were Fluvoxamine, a selective serotonin reuptake inhibitor (SSRI), often prescribed for depression and Ivermectin, used to treat parasitic infections. These medications are already approved by the U.S. Food and Drug Administration for the treatment of other diseases or conditions. This is a nationwide double-blind Randomised Trial to Evaluate Efficacy of Repurposed Medications. The study expected to enrol nearly 15,000 participants from across the U.S.
- On 17th February 2022, South African Health Products Regulatory Authority (SAHPRA) has authorised, with conditions, the importation of molnupiravir 200mg capsules ("LAGEVRIO"). In a phase 2/3 clinical trial, molnupiravir was shown to reduce the risk of hospitalisation or death compared with placebo, but only when treatment was initiated within 5 days of the first symptoms of COVID-19. Molnupiravir is only indicated for use in patients aged 18 years and older with mild to moderate COVID 19. Clinical trial registration #: (NCT04575597).

Immunotherapies trials:

- On 21st February 2022, Synairgen announced the international Phase 3 SPRINTER trial of SNG001 in patients hospitalised with COVID-19 did not meet the primary or key secondary efficacy endpoints. SNG001 is a formulation for inhalation containing the broad-spectrum antiviral protein interferon beta. A total of 623 patients were randomised to receive SNG001 (n=309) or placebo (n=314) in addition to standard of care (SOC). The primary analysis was conducted in the intention-to-treat population (ITT; all randomised patients). The per protocol (PP) population excludes patients with major protocol violations that may have confounded the results. SNG001 demonstrated a favourable safety profile and was well tolerated. Patients who received SNG001 were no more likely to be discharged from hospital than patients who received placebo, and patients who received SNG001 were also no more likely to recover to 'no limitation of activities' than patients who received placebo, in both the ITT and PP populations. Clinical trial registration #: (NCT04732949).

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

Contributors

In alphabetical order:

Alimi, Yewande; Bouesso, Berence Ouaya; Camara, Neema; Dadji, Kwami Hoenoukpo; Hussein, Ally K; Kishimba, Rogath S; Loembé, Marguerite Massinga; Onwuekwe, Ezinne; Seydi, Aminata; Sounga, Carine Sylvie; Sy, Sokona; Tshangela, Akhona; Waya, Chimwemwe; Wangou, Monde Mambimongo.

For any queries, kindly contact: Akhona Tshangela (AkhonaT@africa-union.org)