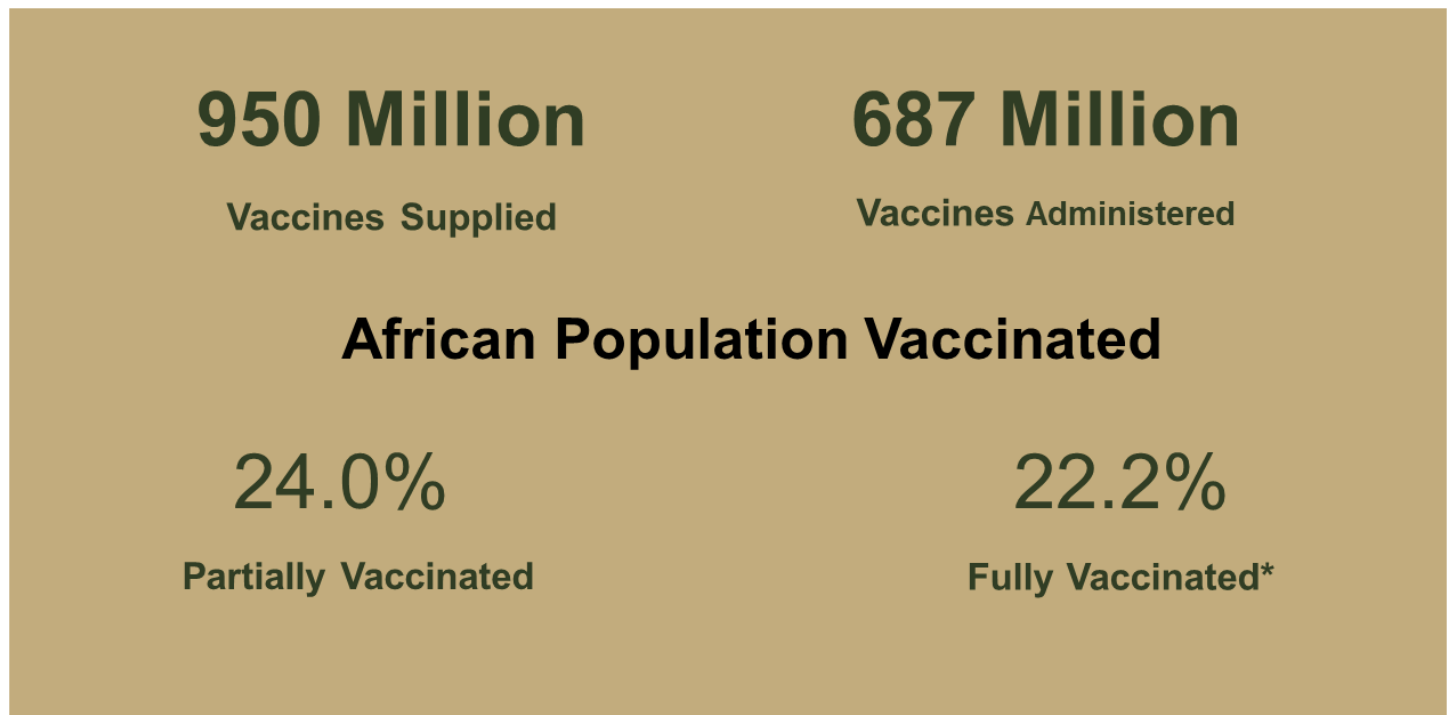


COVID-19 Scientific and Public Health Policy Update¹ (14 September 2022)

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 14 September 2022

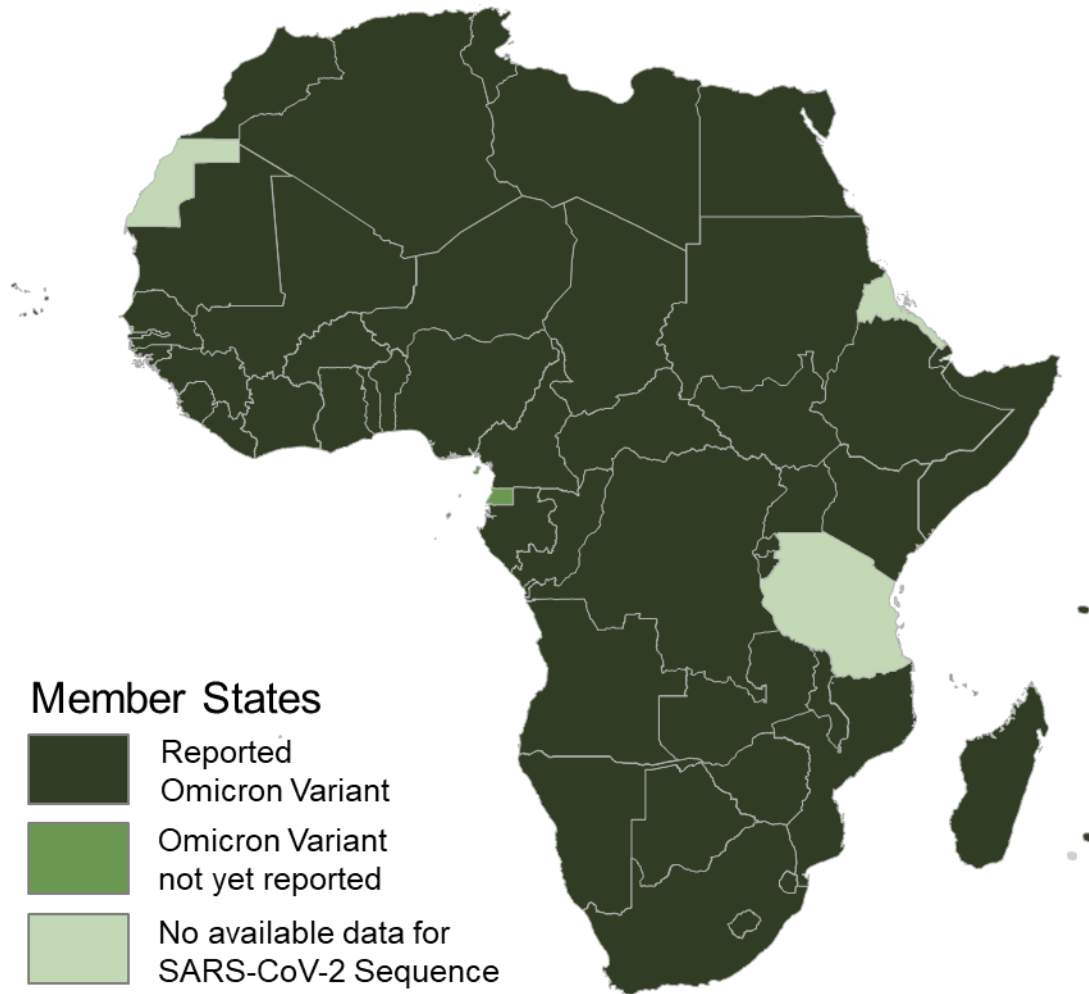
Note:

- 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 14 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 14 September 2022

B. New guidelines and resources

Since 30 August 2022,

- Africa CDC² has published new guidance and resources on:
 - [Outbreak Brief 138: Coronavirus Disease 2019 \(COVID-19\) Pandemic](#)
- U.S. CDC³ has published new guidance and resources on:
 - [CDC Recommends the First Updated COVID-19 Booster](#)
 - [Duration of Isolation and Precautions for Adults with COVID-19](#)
 - [Frequently Asked Questions about COVID-19 Vaccination in Children](#)
 - [How to Select, Wear, and Clean Your Mask](#)

² Africa CDC: Africa Centres for Disease Control and Prevention

³ U.S. CDC: United States Centres for Disease Control and Prevention

- [Wearing Masks in Travel and Public Transportation Settings](#)
- [Post-COVID Conditions: CDC Science](#)
- WHO⁴ has published new guidance and resources on:
 - [Framework and toolkit for infection prevention and control in outbreak preparedness, readiness and response at the health care facility level](#)
 - [Imagining the future of pandemics and epidemics: a 2022 perspective](#)
 - [Progress on WASH in health care facilities 2000-2021: Special focus on WASH and infection prevention and control \(IPC\)](#)
- U.S. FDA⁵ has issued press releases on:
 - [On 31 August, FDA authorised Moderna, Pfizer-BioNTech Bivalent COVID-19 Vaccines for use as a booster dose](#)
 - [As of 13 September, 438 tests and sample collection devices are authorised by the FDA under emergency use authorisations \(EUAs\)](#)
- ECDC⁶ has issued new resources on:
 - [Overview of the implementation of COVID-19 vaccination strategies and deployment plans in the EU/EEA](#)
- UKHSA⁷ has issued new guidance and press releases on:
 - [Investigation of SARS-CoV-2 variants: technical briefings](#)
 - [SARS-CoV-2 variants of public health interest](#)
 - [COVID-19: information and advice for health and care professionals](#)
 - [JCVI advises use of additional bivalent vaccine for autumn booster campaign](#)
 - [Consensus statements and medium-term projections on COVID-19](#)

C. Scientific updates

Basic Science

- This [animal study](#) in Denmark evaluated airway mucosal immune responses following administration of a parenteral prime – intranasal boost vaccine regimen in Syrian hamsters. The authors administered 2 immunizations with Spike HexaPro trimer formulated in a cationic liposomal adjuvant 21 days apart. Immunization by parenteral prime – intranasal boost induced anti-spike IgG and SARS-CoV-2 neutralising antibody responses in serum and elicited IgA responses in the upper respiratory tract. In a transmission model in which vaccinated contacts were co-housed with SARS-CoV-2 infected index hamsters, the parenteral prime-mucosal boost strategy lowered virus titres in the upper airways and protected against onward transmission. These results suggest that a parenteral prime - intranasal boost vaccine strategy may be an effective means to limit virus spread in the population.
- This [study](#) in the United States used COVID-19 patient databases and cell culture to identify that the macrophage-induced cytokine storm was linked to Type I interferons (IFN-I) signalling in patient lungs. Plasmacytoid dendritic cells (pDCs) were the main producers of IFN-I, because they were directly infected with SARS-CoV-2, which triggered Toll-like receptor 7 (TLR7) activation. This IFN-I made macrophages more responsive to environmental stimuli, thus triggering the production of multiple cytokines. Thus, the authors present a mechanism whereby pDCs are infected by SARS-CoV-2,

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

subsequently producing IFN-I, and stimulating a macrophage-mediated cytokine storm during SARS-CoV-2 infection.

- This [review](#) describes the immune response and evasion mechanisms of Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Kappa (B.1.617.1), Delta (B.1.617.2) and Omicron (B.1.1.529) variants of SARS-CoV-2. The immune responses and evasion mechanisms could provide some helpful advices for future vaccine development.

Vaccines

- This [randomised, double-blind, placebo-controlled, phase 3 trial](#) in Belgium, Brazil, Colombia, France, Germany, the Philippines, South Africa, Spain, the UK, and the USA assessed the efficacy, safety, and immunogenicity of the Ad26.COV2.S vaccine (Janssen) as primary vaccination plus a booster dose. The study involved 31,300 participants, 14,492 of whom received two doses (7,484 in the Ad26.COV2.S group and 7,008 in the placebo group). Vaccine efficacy was 75.2% (adjusted 95% CI 54.6–87.3) against moderate to severe–critical COVID-19. Most cases were due to the variants alpha (B.1.1.7) and mu (B.1.621); endpoints for the primary analysis accrued from 16 November 2020 to 25 June 2021, before the global dominance of delta (B.1.617.2) or omicron (B.1.1.529). The booster vaccine exhibited an acceptable safety profile. The overall frequencies of solicited local and systemic adverse events were higher among vaccine recipients than placebo recipients after the primary and booster doses. The frequency of solicited adverse events in the Ad26.COV2.S group were similar following the primary and booster vaccinations (local adverse events, 1676 [55.6%] of 3015 vs 896 [57.5%] of 1559, respectively; systemic adverse events, 1764 [58.5%] of 3015 vs 821 [52.7%] of 1559, respectively). Solicited adverse events were transient and mostly grade 1–2 in severity.
- This [modelling study](#) conducted across 47 countries assessed how the number of COVID-19 vaccines secured correlates with the vaccination coverage (full and booster) depending on whether there is trust in national government or not. The model includes an interaction term of the two key variables, also controls for a range of socio-economic factors and country specific variables. The results indicate a non-linear and mixed relationship between the numbers secured, the public trust, and the vaccination rate. In Feb. 2022, with confidence in government, securing number of vaccines to cover 200% of the population (or more) increased the full vaccination rate by 12.26% (95% CI: 11.70 - 12.81); where number secured was 300% (or more), the coverage increased by 7.46% (95% CI: 6.95 - 7.97). Under similar scenarios, rate of booster shots increased by 13.16% (95% CI: 12.62 - 13.70; $p < 0.01$) and 14.36% (95% CI: 13.86 - 14.85; $p < 0.01$), respectively. Where the number secured fell below 200%, confidence in government had a reverse relationship with the rate of full vaccination (-2.65; 95% CI: -3.32 - -1.99), yet positive with the rate of booster shots (1.65; 95% CI: 1.18 - 2.12). These results indicate that better success can be achieved by a combination of factors including securing sufficient number of vaccines and also ensuring the public trust. Vaccine abundance, however, cannot be translated into greater success in vaccination coverage. This study highlights the importance of efficiency in acquiring vaccine resources and need for improvement in public belief in immunization programmes rather than stock piling.
- This [prospective cohort study](#) in the United States assessed reactions to the booster or 3rd dose of the COVID-19 vaccine and vaccine experiences among pregnant and lactating individuals. The study involved 17,014 participants; of these 2,009 (11.8%) were pregnant, 10,279 (60.4%) were lactating, and 4726 (27.8%) were neither pregnant nor lactating at the time of their booster or third dose. After a COVID-19 booster or third dose, most individuals (14,074/17,005 [82.8%]) reported a local reaction, and 11,542/17,005 (67.9%) reported at least 1 systemic symptom. Compared with individuals who were neither pregnant nor lactating, pregnant participants were more likely to report any local reaction to a COVID-19 booster or 3rd dose (adjusted odds ratio [aOR], 1.2; 95% CI, 1.0-1.4; $p = 0.01$) but less likely to report any systemic reaction (aOR, 0.7; 95% CI, 0.6-0.8; $p < 0.001$). Most pregnant (1,961/ 2,009 [97.6%]) and lactating (9,866/10,277 [96.0%]) individuals reported no obstetric or lactation concerns after vaccination. This study suggests that COVID-19 vaccine boosters or 3rd doses were well tolerated among pregnant and lactating individuals.

- This [cohort study](#) in the United Kingdom assessed the immune responses to 3rd and 4th doses of heterologous and homologous vaccines in a kidney transplant population. The study involved 724 kidney transplant recipients who received mRNA vaccines. A significant proportion (24.1% and 18.8%) of kidney transplant recipients without prior natural infection, do not have any detectable spike protein antibody in response to 3rd and 4th doses of vaccine respectively. T cell responses are poor following fourth dose vaccination regardless of prior infection status. In contrast to three-dose vaccination, there was no benefit of heterologous dosing schedule on either the proportion or magnitude of serological responses. Alternative strategies are required to provide protection to this vulnerable group.
- This [exploratory study](#) in the United Kingdom used a crowdsourcing approach (1) to solicit existing interventions worldwide and propose new ones to increase COVID-19 booster vaccine uptake, and (2) to assess the perceived effectiveness and acceptability of these interventions. The study was conducted in 2 phases: In the first phase (December 2021), international experts ($n = 78$ from 17 countries) proposed 46 unique interventions. In the second phase (January 2022), experts ($n = 307$ from 34 countries) and representative general population samples from the UK ($n = 299$) and the US ($n = 300$) rated the proposed interventions on several evaluation criteria. Sanctions were evaluated as potentially most effective but least accepted. Evaluations by expert and general population samples were considerably aligned. Interventions that received the most positive evaluations regarding both effectiveness and acceptability across evaluation groups were: a day off work after getting vaccinated, financial incentives, tax benefits, promotional campaigns, and mobile vaccination teams. These results provide useful insights to help governmental and non-governmental institutions in their decisions about which interventions to implement.

Diagnostics

- This [modelling study](#) in the United States developed an Intelligent Testing Allocation (ITA) method by leveraging data from the CovIdentify study (6,765 participants) and the MyPHD study (8,580 participants), including smartwatch data from 1265 individuals of whom 126 tested positive for COVID-19. They found that resting heart rate (RHR) features distinguished between COVID-19-positive and -negative cases earlier in the course of the infection than steps features, as early as 10 and 5 days prior to the diagnostic test, respectively. They also found that including steps features increased the area under the receiver operating characteristic curve (AUC-ROC) by 7–11% when compared with RHR features alone, while including RHR features improved the AUC of the ITA model's precision-recall curve (AUC-PR) by 38–50% when compared with steps features alone. They found that ITA generated up to a 6.5-fold increase in the positivity rate in the cross-validated training set and up to a 4.5-fold increase in the positivity rate in the independent test set, including both symptomatic and asymptomatic (up to 27%) individuals. These findings suggest that, if deployed on a large scale and without needing self-reported symptoms, the ITA method could improve the allocation of diagnostic testing resources and reduce the burden of test shortages.
- This [study](#) in the United Kingdom assessed whether the sensitivity of the Innova lateral flow test (LFT) is dependent on the viral load and on the location of swabbing in the respiratory tract in children. The study involved a total of 470 paired swabs from children (<18 years) in 2 phases. Phase 1 (routine testing): 435 paired swabs taken in 431 asymptomatic patients resulted in 8 positive RT-PCRs, 9 PCR test failures and 418 negative RT-PCRs from nose and throat (NT) or endotracheal (ET) swabs. The test performance of anterior nasal (AN) LFT demonstrated sensitivity: 25% (4%–59%), specificity: 100% (99%–100%), positive predictive value (PPV): 100% (18%–100%) and negative predictive value (NPV): 99% (97%–99%). Phase 2 (testing known SARS-CoV-2 positive): 14 AN RT-PCR-positive results demonstrated a sensitivity of 77% (50%–92%) of LFTs performed on AN swabs. 15/16 paired buccal LFT swabs were negative. These findings suggest that the sensitivity of LFTs may improve with specimens both taken from the same location (in this study anterior nares) but buccal swabbing is not an appropriate LFT specimen.

Care and Treatment

- This [retrospective cohort study](#) in Mexico assessed the usefulness of leukocyte glucose index (LGI) as a biomarker for severe COVID-19. The study involved 109 COVID-19 patients with a positive nucleic acid test for SARS-CoV-2 from April to July 2020 at a third level reference hospital in Veracruz. LGI was identified as an independent risk factor (odds ratio [OR] = 1.727, 95% confidence interval [CI]: 1.026–3.048, $p=0.041$), with an area under the curve (AUC) of 0.749 (95% CI: 0.642–0.857, $p<0.0001$). Interestingly, LGI was a potential risk factor (OR = 2.694, 95% CI: 1.575–5.283, $p_{corrected} < 0.05$) for severe COVID-19 in female but not in male patients. In addition, LGI proved to be a strong predictor of the severity in patients with diabetes (AUC = 0.915 (95% CI: 0.830–1), sensitivity = 0.833, and specificity = 0.931). The AUC of LGI, together with the respiratory rate (LGI + RR), showed a considerable improvement (AUC = 0.894, 95% CI: 0.835–0.954) compared to the other biochemical and respiratory parameters analysed. Together, these findings indicate that LGI could potentially be used as a biomarker of severity in COVID-19 patients.
- This [multicentre cohort study](#) assessed the potential applications of the urinary proteomic COV50 biomarker (identified in the CRIT-CoV-U pilot study) in clinical practice and trial design. The study involved 1012 adults with PCR confirmed COVID-29 from 8 European countries (Austria, France, Germany, Greece, North Macedonia, Poland, Spain, and Sweden). COV50 consists of 50 differentially regulated urinary peptides and is able to predict death and disease progression in adults with mild-to-moderate PCR-confirmed COVID-19 infection. The predictive accuracy of the optimised COV50 thresholds was 74.4% for mortality and 67.4% for disease progression. When adjusted for covariables and then the baseline WHO score, the continuously distributed urinary marker and its optimised thresholds improved the area under the curves from 0.835 to 0.854 to 0.853 for death and from 0.697 to 0.740 to 0.730 for disease progression. Using the 0.04 threshold to differentiate low COVID-19-associated risk from high COVID-19-associated risk would allow selecting patients with mild disease at presentation for earlier drug treatment, thereby decreasing the risk of worsening disease and death and reducing hospitalisation costs.
- This [case-control study](#) in China describes the systemic metabolic signatures of survivors of non-severe COVID-19 at six months after discharge using metabolomics approaches. The study included 21 cases (non-severe COVID-19) and 22 controls (without SARS-CoV-2 infection) from Renmin Hospital of Wuhan University. The serum amino acids, organic acids, purine, fatty acids and lipid metabolism were still abnormal in the survivors, but the kynurenine pathway and the level of itaconic acid have returned to normal. These metabolic abnormalities are associated with liver injury, mental health, energy production, and inflammatory responses. Their findings provide information on biomarkers and therapeutic targets of infection and cues for post-hospital care and intervention strategies centred on metabolism reprogramming.

Epidemiology

- This [case series](#) in the United States evaluated the application of a statistical learning strategy (SLS) to improve early detection of novel SARS-CoV-2 variants using viral sequence data from global surveillance. The study involved 2,698 Omicron cases in Africa and 12,141 Omicron cases in the United States. The SLS found that Omicron was dynamically expanding with trackable expansion over time. The results indicated that Omicron could have been detected 20 days earlier in Africa; similarly, 8 Omicron cases were detected in the United States by November 25, 2021, prior to the official US Centers for Disease Control and Prevention declaration. These findings suggest that novel data analytics such as statistical learning strategy may have applications for surveillance of SARS-CoV-2 variants.
- This [cohort study](#) in Italy assessed the 2-year prevalence and recovery rate of smell or taste dysfunction in mildly symptomatic COVID-19 patients. The study involved 168 adults who were treated at Treviso General Hospital and tested positive for SARS-CoV-2 by PCR in March 2020. Among the 119 patients with onset of COVID-19-associated smell or taste dysfunction within 4 weeks, 105 (88.2%; 95% CI, 81.0%–93.4%) reported complete resolution at 2 years, 11 (9.2%; 95% CI, 4.7%–15.9%) reported a

decrease in the severity, and 3 (2.5%; 95% CI, 0.5%-7.2%) reported the symptom was unchanged or worse; a late recovery (>6 months after the onset) was reported in 13 patients (10.9%; 95% CI, 5.9%-18.0%). At 2-year follow-up, the most frequent non-chemosensory symptoms were fatigue (n = 31; 18.5%; 95% CI, 12.9%-25.2%), followed by shortness of breath (n = 18; 10.7%; 95% CI, 6.5%-16.4%). Overall, the persistence of at least 1 symptom at 2-year follow-up was reported by 47 patients (28.0%; 95% CI, 21.3%-35.4%).

- This [population-based cohort study](#) in the England assessed risk factors for post-booster omicron COVID-19 deaths. The study involved 19,473,570 individuals aged 18 to 100 years living in England who had completed both doses of their primary vaccination schedule and had received their mRNA booster 14 days or more prior to 31 December 2021. The outcome of interest was time to death involving COVID-19 occurring between 1 January and 16 March 2022. There were 4,781 (0.02%) deaths involving COVID-19 and 58,020 (0.3%) deaths from other causes. Age was the most important characteristic associated with the risk of post-booster COVID-19 death with an HR of 31.3 (95% CI, 26.1-37.6) for an 80-year-old individual compared with a 50-year-old. Women were at lower risk than men (HR, 0.52; 95% CI, 0.49-0.55). Living in a care home or in a socioeconomically deprived area were also associated with increased risk of COVID-19 death. Risk was particularly elevated for people with severe combined immunodeficiency (HR, 6.2; 95% CI, 3.3-11.5). These results identify subpopulations with the highest risk of death and should be considered a priority for COVID-19 therapeutics and further booster doses.
- This [time series analysis](#) in South Africa proposes quantifying COVID-19 case-to-hospitalisation and case-to-death lag intervals using surveillance data not only for research purposes, but also for timely and feasible estimation of the relative severity of novel variants, by age or other stratifying factors. The study utilised a total of 3,569,621 cases, 494,186 hospitalisations, and 99,954 deaths attributable to COVID-19 in the analyses. Fluctuations in cases were generally followed by a similar trend in hospitalisations within 7 days and deaths within 15 days. They noted a marked reduction in disease severity throughout the omicron period relative to previous waves (age-standardised case-fatality ratios were consistently reduced by >50%), most substantial for age strata with individuals 50 years or older. Their proposed methodology is an accessible tool that can be added to currently deployed approaches for attaining a comprehensive understanding of the threat of a novel variant.
- This [meta-analysis](#) assessed risk factors among pregnant and postpartum women with COVID-19 for adverse outcomes related to: disease severity, maternal morbidities, neonatal mortality and morbidity, adverse birth outcomes. The study included 21,977 cases of SARS-CoV-2 infection in pregnancy or postpartum from 33 countries and territories. Women with comorbidities (pre-existing diabetes, hypertension, cardiovascular disease) versus those without were at higher risk for COVID-19 severity and pregnancy health outcomes (foetal death, preterm birth, low birthweight). Participants with COVID-19 and HIV were 1.74 times (95% CI: 1.12, 2.71) more likely to be admitted to the ICU. Pregnant women who were underweight before pregnancy were at higher risk of ICU admission (RR 5.53, 95% CI: 2.27, 13.44), ventilation (RR 9.36, 95% CI: 3.87, 22.63), and pregnancy-related death (RR 14.10, 95% CI: 2.83, 70.36). Pre-pregnancy obesity was also a risk factor for severe COVID-19 outcomes including ICU admission (RR 1.81, 95% CI: 1.26, 2.60), ventilation (RR 2.05, 95% CI: 1.20, 3.51), any critical care (RR 1.89, 95% CI: 1.28, 2.77), and pneumonia (RR 1.66, 95% CI: 1.18, 2.33). Anaemic pregnant women with COVID-19 also had increased risk of ICU admission (RR 1.63, 95% CI: 1.25, 2.11) and death (RR 2.36, 95% CI: 1.15, 4.81). Special priority for prevention and treatment should be given to pregnant women with these additional risk factors.

Infection Prevention & Control

- This [open-label, randomized controlled trial](#) in Japan assessed the potential infection risk among individuals who handle linen used by SARS-CoV-2-infected people. The authors examined 700 samples from 13 SARS-CoV-2-infected participants and their surrounding environment. SARS-CoV-2 RNA was detected from 14% (52/362) of the linens used by COVID-19 patients (cycle threshold [Ct] value: 33–40). SARS-CoV-2 RNA was detected from 8% (2/26) of rinse water after washing or disinfection, from 15% (16/104) of air samples in the workspace, and from 10% (5/52) of gowns worn

by linen-handling people, all with high Ct values (> 36). The potential risk of SARS-CoV-2 infection from handling linens used by SARS-CoV-2-infected people exists but appears to be low.

Non-pharmaceutical interventions, social distancing

- None

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 13 September 2022, [Novavax and Serum Institute of India announced that the South African Health Products Regulatory Authority has granted full product registration with conditions for Novavax' protein-based vaccine, NVX-CoV2373, as a two-dose primary series for active immunization to prevent COVID-19 in adults aged 18 and older.](#) The product registration was based on the totality of preclinical, manufacturing, and clinical trial data submitted for review. This includes two pivotal Phase 3 clinical trials: PREVENT-19, which enrolled 29,960 participants aged 18 years and older in the U.S. and Mexico. In both trials, the vaccine demonstrated efficacy with a reassuring safety and tolerability profile. Serious and severe adverse events were low in number and balanced between vaccine and placebo groups. Clinical trial registration #: (NCT04611802).
- On 12 September 2022, [Pfizer and BioNTech announced a 30-µg booster dose of Omicron BA.4/BA.5 bivalent-adapted COVID-19 Vaccine \(COMIRNATY Original/Omicron BA.4/BA.5 15/15 µg\) has been recommended for conditional marketing authorisation \(cMA\) by the European Medicines Agency's \(EMA\) Committee for Medicinal Products for Human Use \(CHMP\) for individuals ages 12 years and older.](#) The Omicron BA.4/BA.5-adapted bivalent vaccine contains 15-µg of mRNA encoding the wild-type spike protein of SARS-CoV-2 in the Original Pfizer-BioNTech COVID-19 Vaccine, and 15-µg of mRNA encoding the spike protein of the Omicron BA.4/BA.5 subvariants. Apart from the addition of the mRNA sequence of the BA.4/BA.5 spike protein, all other components of the vaccine remain unchanged. The CHMP recommendation based on data from Omicron BA.1-adapted bivalent vaccine as well as pre-clinical and manufacturing data from the Omicron BA.4/BA.5-adapted bivalent vaccine. Clinical data from a Phase 2/3 trial showed a booster dose of Pfizer and BioNTech's Omicron BA.1-adapted bivalent vaccine elicited a superior immune response against the Omicron BA.1 subvariant compared to the Pfizer's current COVID-19 vaccine, with a favourable safety profile. Additionally, pre-clinical data showed a booster dose of the BA.4/BA.5-adapted bivalent vaccine generated a strong neutralising antibody response against the Omicron sub lineages including BA.1, BA.2, BA.4 and BA.5 subvariants, as well as the original virus, while retaining a favourable safety profile. Clinical trial registration #: (NCT04816643).
- On 12 September 2022, [Novavax announced the European Commission \(EC\) has approved the expanded conditional marketing authorisation \(CMA\) of Nuvaxovid \(NVX-CoV2373\) COVID-19 vaccine in the European Union \(EU\) as a homologous and heterologous booster for active immunization to prevent COVID-19 for adults aged 18 and older.](#) The expanded CMA was based on 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 robust antibody response when used as a heterologous third booster dose. Clinical trial registration #: (NCT05372588).
- On 6 September 2022, [Bharat announced that iNCOVACC \(BBV154\), has received approval under Restricted Use in Emergency Situation for ages 18 and above. iNCOVACC is a recombinant replication deficient adenovirus vectored vaccine with a prefusion stabilized spike protein.](#) This vaccine candidate was evaluated in phase 1, 2 and 3 clinical trials with successful results. iNCOVACC has been specifically formulated to allow intranasal delivery through nasal drops. The nasal delivery system has been designed and developed to be cost effective in low- and middle-income countries. iNCOVACC was developed in partnership with Washington University St. Louis, which had designed and developed

the recombinant adenoviral vectored constructs and evaluated them in preclinical studies for efficacy. Product development related to preclinical safety evaluation, large scale manufacturing scale up, formulation and delivery device development, including human clinical trials were conducted by Bharat Biotech. Clinical trials were conducted to evaluate iNCOVACC as a primary dose schedule, as heterologous booster dose for subjects who have previously received 2 doses of the two commonly administered covid vaccines in India. Immunogenicity was evaluated through serum neutralising antibodies by P RNT assays and serum IgG's through ELISA's. Clinical trial registration #: (NCT05522335 & NCT04751682).

- On 5 September 2022, [CanSino announced that the National Medical Products Administration of China \("NMPA"\) has granted the approval for its Recombinant COVID-19 Vaccine \(Adenovirus Type 5 Vector\) for Inhalation \(Convidecia Air\) to be used as a booster dose.](#) Utilizing the same adenovirus vector technological platform as the intramuscular version Convidecia, Convidecia Air provides a non-invasive option that uses a nebulizer to change liquid into an aerosol for inhalation through the mouth. Convidecia Air is needle-free and can effectively induce comprehensive immune protection in response to SARS-CoV-2 after just one breath. Studies demonstrated that Convidecia Air could prompt robust cellular, humoral and mucosal immunity to attain triple protection as well as control the virus spread and the infection. Clinical trial registration #: (NCT05517642).
- On 2 September 2022, [Novavax announced that Swissmedic, the Swiss Agency for Therapeutic Products, has expanded its temporary authorisation of Nuvaxovid \(NVX-CoV2373\) COVID-19 vaccine in Switzerland for active immunization to prevent COVID-19 in adolescents aged 12 through 17 and as a heterologous and homologous booster dose for adults aged 18 and older.](#) The authorisation for adolescents aged 12 through 17 is based on data from the ongoing paediatric expansion of the Phase 3 PREVENT-19 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 paediatric expansion, Nuvaxovid achieved its primary efficacy 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. Preliminary safety data from the paediatric expansion showed the vaccine to be generally well-tolerated. Serious and severe adverse events were low in number and balanced between vaccine and placebo groups, and not considered related to the vaccine. Clinical trial registration #: (NCT04611802).
- On 01 September 2022, [Novavax announced that Nuvaxovid \(NVX-CoV2373\) COVID-19 vaccine has been recommended for expanded conditional marketing authorisation \(CMA\) in the European Union \(EU\) as a homologous and heterologous booster for active immunization to prevent COVID-19 for adults aged 18 and older.](#) The CHMP of the European Medicines Agency based its opinion on results from two Phase 2 trials, and the UK-sponsored COV-BOOST trial. In 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 robust antibody response when used as a heterologous third booster dose. In the Novavax-sponsored trials, following the booster, local and systemic reactions were generally short-lived with a median duration of approximately two days. The incidence of Grade 3 or higher events remained relatively low. Clinical trial registration #: (NCT05372588).
- On 01 September 2022, [Moderna announced that Health Canada has authorised the use of its Omicron-targeting bivalent COVID-19 booster vaccine, mRNA-1273.214 \(Spikevax Bivalent Original/Omicron\) as a booster dose for active immunization against COVID-19 in individuals 18 years of age and older.](#) Spikevax Bivalent Original/Omicron is a next-generation bivalent vaccine that targets both the original strain of SARS-CoV-2 and the Omicron variant of concern (BA.1). The decision based on clinical trial data from a phase 2/3 trial, in which mRNA-1273.214 met all primary endpoints, including superior neutralising antibody response against Omicron (BA.1) when compared to a 50µg booster dose of mRNA-1273 in baseline seronegative participants. A booster dose of mRNA-1273.214 increased neutralising geometric mean titres (GMT) against Omicron approximately 8-fold above baseline levels. Additional analysis showed mRNA-1273.214 elicited potent neutralising antibody responses against the Omicron subvariants BA.4 and BA.5 compared to the currently authorised

booster (mRNA-1273) regardless of prior infection status or age. Clinical trial registration #: (NCT05249829).

- On 31 August 2022, [the U.S. Food and Drug Administration amended the emergency use authorisations \(EUAs\) of the Moderna COVID-19 Vaccine and the Pfizer-BioNTech COVID-19 Vaccine to authorise bivalent formulations of the vaccines for use as a single booster dose at least two months following primary or booster vaccination.](#) The bivalent vaccines, which are also referred to as “updated boosters,” contain two messenger RNA (mRNA) components of SARS-CoV-2 virus, one of the original strain of SARS-CoV-2 and the other one in common between the BA.4 and BA.5 lineages of the omicron variant of SARS-CoV-2. The Moderna COVID-19 Vaccine, Bivalent, is authorised for use as a single booster dose in individuals 18 years of age and older. The Pfizer-BioNTech COVID-19 Vaccine, Bivalent, is authorised for use as a single booster dose in individuals 12 years of age and older. The FDA analysed immune response data among approximately 600 individuals 18 years of age and older who had previously received a two-dose primary series and one booster dose of monovalent Moderna COVID-19 Vaccine to evaluate its effectiveness. After 28 days, the immune response against BA.1 of the participants who received the bivalent vaccine was better than the immune response of those who had received the monovalent Moderna COVID-19 Vaccine. To evaluate the effectiveness of a single booster dose of the Pfizer-BioNTech COVID-19 Vaccine, Bivalent for individuals 12 years of age and older, the FDA analysed immune response data among approximately 600 adults greater than 55 years of age who had previously received a 2-dose primary series and one booster dose with the monovalent Pfizer-BioNTech COVID-19 Vaccine. After one month, the immune response against BA.1 of the participants who received the bivalent vaccine was better than the immune response of those who had received the monovalent Pfizer-BioNTech COVID-19 Vaccine. Both, Moderna and Pfizer-BioNTech investigational bivalent COVID 19 were within safe profile.

Therapeutics trials:

- On 13 September 2022, [Pardes Biosciences reported commencement of a Phase 2 double-blind, randomized study to evaluate the antiviral activity, safety, and efficacy of orally administered PBI-0451 compared with placebo in non-hospitalised symptomatic adults with COVID-19 who are not at increased risk of progressing to severe illness.](#) PBI-0451 is a potential stand-alone, novel direct-acting, oral antiviral drug candidate for the treatment and prevention of SARS-CoV-2 infections and associated diseases. PBI-0451 inhibit the main cysteine protease (Mpro) of all known coronaviruses, including SARS-CoV-2. The phase 2 expects to enrol 210 patients at approximately 75 sites within the United States. Study eligibility includes symptoms of COVID-19 for 5 or less days and a positive test for SARS-CoV-2 infection. Use of concomitant medications for underlying health conditions is not restricted in the clinical trial. Participants will be administered PBI-0451 orally with food, twice daily, at a 700 mg (2x 350 mg tablets) dose or placebo over five days. The primary objective is to determine the proportion of patients below the limit of detection in nasal swab samples for infectious SARS-CoV-2 on day three. Secondary objectives include assessments of safety and tolerability, time to sustained clinical recovery through day 28 defined as key COVID-19 symptoms, and hospitalisations and deaths. In a Phase 1 clinical trial, PBI-0451 at single and multiple doses demonstrated favourable tolerability without any study drug discontinuations and there were no treatment emergent drug-related adverse events assessed as greater than mild in severity. Clinical trial registration #: (NCT05011812).
- On 09 September 2022, [Gladstone Institutes in the US reported a new antiviral therapy called therapeutic interfering particle \(TIP\) developed to offer protection against severe Covid-19 was shown to cut the amount of virus shed from infected animals in a study.](#) The new therapy which is a single-dose administered intranasally was also found to cut down the SARS-CoV-2 virus transmission since it decreases viral shedding. In the study, the team treated Covid-19-infected hamsters with antiviral TIPs and analysed the amount of virus in their noses on a daily basis. TIP-treated animals had fewer viruses in nasal passages at each time point versus hamsters (control animals) that did not receive the treatment. All animals in the control arm were found to be shedding greater levels of the virus by the fifth day, while the virus was not detectable in four out of five animals that received TIP. Treating infected hamsters with TIPs was not found to completely prevent Covid-19 transmission when they

were housed with uninfected animals. However, the freshly exposed hamsters showed to have substantially reduced viral loads and milder disease symptoms.

- On 6 September 2022, [Tetra Bio-Pharma and Cellvera announced to jointly develop ARDS-003 as an oral combination therapeutic candidate with 400mg Qifenda \(Favipiravir\) for Covid-19](#). A first-in-human drug product, ARDS-003 contains the active pharmaceutical agent, Onternabez. Onternabez is a selective full agonist of the type 2 cannabinoid receptor (CB2R). Based on findings from the Prepaire, an artificial intelligence (AI)-based in-silico drug discovery platform, the Favipiravir plus ARDS-003 combination is expected to offer viral clearance. ARDS-003, in preclinical studies, was found to lower the hyperinflammatory response and decelerate the progression of the disease. In the humanised ACE2 mouse model, ARDS-003 monotherapy showed to lower morbidity and mortality signs, including respiratory distress after Covid-19 in a dose-dependent manner, versus placebo. It is claimed to have outperformed an antiviral drug in lowering various proinflammatory mediators linked to hyperinflammation and dysfunction of the immune system after viral infection.

Immunotherapies trials:

- None

Contributors

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