

# COVID-19 Scientific and Public Health Policy Update<sup>1</sup> (6 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 6 July 2022

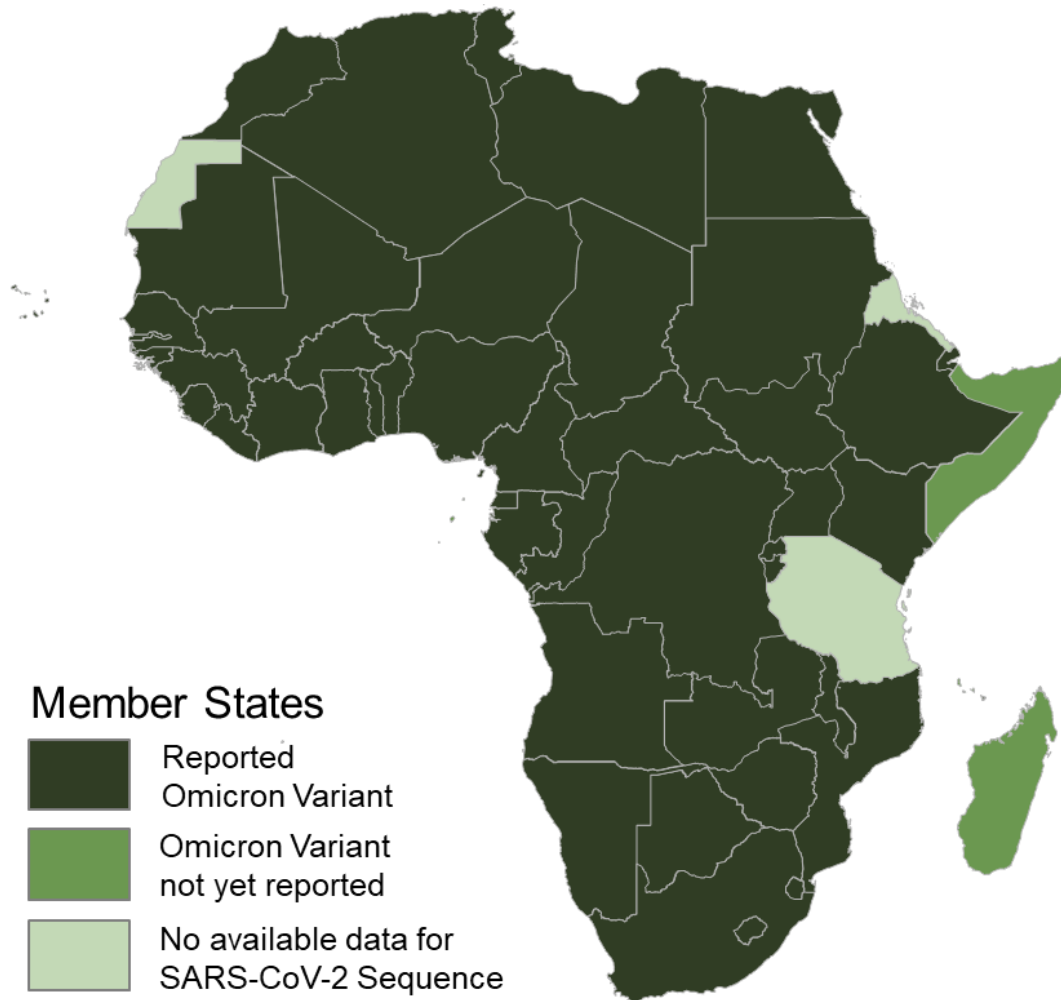
**Note:** Africa CDC has changed the denominator of the calculation for percentage fully vaccinated from 2020 population to 2022 population estimates (UNFPA) to give accurate projections from effective population size (Ne) perspectives.

The resulting effect is that there will be a slight reduction in fully vaccinated coverage percentages of member states and the continent at large.

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

## Variants of Concern (VOC)

The Omicron variant (B.1.1.529), first reported in South Africa on 24<sup>th</sup> November 2021, has spread to 198 countries/territories/areas worldwide. As of 6 July 2022, 49 (89.1%) of the 55 Member States in Africa have reported this variant. For more information visit <https://africacdc.org/institutes/africa-pathogen-genomics-initiative/>.



Updated 6 July 2022

## B. New guidelines and resources

Since 21 June 2022,

- Africa CDC<sup>2</sup> has published new guidance and resources on:
  - [Africa CDC – Mastercard Foundation: Saving Lives and Livelihoods Newsletter, June 2022](#)
  - [Outbreak Brief 128: Coronavirus Disease 2019 \(COVID-19\) Pandemic](#)
- U.S. CDC<sup>3</sup> has published new guidance and resources on:
  - [Interim Recommendations of the Advisory Committee on Immunization Practices for Use of Moderna and Pfizer-BioNTech COVID-19 Vaccines in Children Aged 6 Months–5 Years — United States, June 2022](#)

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

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

- [Operational Considerations for Maintaining Essential Services for and Providing Maternal, Newborn, and Child Healthcare in Low-Resource Countries](#)
- [Global Community Mitigation](#)
- [COVID-19 Vaccines for Moderately to Severely Immunocompromised People](#)
- [CDC Recommends Moderna COVID-19 Vaccine for Children and Adolescents](#)
- WHO<sup>4</sup> has published new guidance and resources on:
  - [Multi-sectoral impacts of the COVID-19 pandemic on nutrition outcomes: an analytical framework](#)
  - [Clinical management of COVID-19: Living guideline, 23 June 2022](#)
- U.S. FDA<sup>5</sup> has issued press releases on:
  - [On 30 June, FDA recommended inclusion of Omicron BA.4/5 component for COVID-19 vaccine booster doses](#)
  - [On 29 June, FDA revised the Evusheld Fact Sheet for Healthcare Providers to recommend repeat dosing every six months if patients need ongoing protection](#)
  - [As of 5 July, 438 tests and sample collection devices are authorised by the FDA under emergency use authorisations \(EUAs\)](#)
- ECDC<sup>6</sup> has issued new resources on:
  - [Joint ECDC-WHO Regional Office for Europe Weekly COVID-19 Surveillance Bulletin](#)
- UKHSA<sup>7</sup> has issued new guidance and press releases on:
  - [COVID-19: the future of UKHSA surveillance](#)
  - [High consequence infectious diseases \(HCID\)](#)

## C. Scientific updates

### Basic Science

- This [modelling study](#) in Italy assessed the distribution of the generation time (both intrinsic and realized), realized household serial interval, and contribution of pre-symptomatic transmission for SARS-CoV-2 Omicron variant. The authors analysed data from 23,122 Omicron infections clustered in 8903 households in Reggio Emilia throughout January 2022. They estimated a mean intrinsic generation time of 6.84 days (95% CI, 5.72–8.60), and a mean realized household generation time of 3.59 days (95% CI, 3.55–3.60). The household serial interval was 2.38 days (95% CI, 2.30–2.47) with about 51% (95% CI, 45–56%) of infections caused by symptomatic individuals being generated before symptom onset. Estimates in this study may be useful to design quarantine, isolation and contact tracing protocols and to support surveillance (e.g., for the accurate computation of reproduction numbers).
- This [longitudinal study](#) in the United States characterised viral decay kinetics of the omicron variant and the duration of shedding of the culturable virus. The study involved 66 newly diagnosed outpatients from July 2021 through January 2022. All but 1 participant had symptomatic infection. Sequencing revealed that 32 patients had delta (B.1.617.2), 34 had omicron subvariant BA.1. Following a Cox proportional-hazards model that adjusted for age, sex, and vaccination status was used, the number of days from an initial positive polymerase-chain-reaction (PCR) assay to a negative PCR assay (adjusted hazard ratio, 0.61; 95% CI, 0.33 to 1.15) and the number of days from an initial positive PCR assay to culture conversion (adjusted hazard ratio, 0.77; 95% CI, 0.44 to 1.37) were similar in the two

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

<sup>5</sup> U.S. FDA: United States Food and Drug Administration

<sup>6</sup> ECDC: European Centre for Disease Prevention and Control

<sup>7</sup> UKHSA: United Kingdom Health Security Agency

variant groups. The median time from the initial positive PCR assay to culture conversion was 4 days (interquartile range [IQR], 3 to 5) in the delta group and 5 days (IQR, 3 to 9) in the omicron group; the median time from symptom onset or the initial positive PCR assay, whichever was earlier, to culture conversion was 6 days (IQR, 4 to 7) and 8 days (IQR, 5 to 10), respectively. There were no appreciable between-group differences in the time to PCR conversion or culture conversion according to vaccination status, although the sample size was quite small.

- This [longitudinal observational study](#) in Croatia and the United Kingdom assessed whether severity and duration of COVID-19 are associated with altered IgG glycosylation. The authors analysed the composition of total IgG N-glycome in 154 patients with COVID-19 (108-Severe, 46-mild) from four independent cohorts. The IgG glycome in severe COVID-19 patients was found to be significantly altered in a way that it indicates decreased immunosuppressive action of circulating immunoglobulins. The magnitude of observed changes is associated with the severity of the disease, indicating that aberrant IgG glycome composition or changes in IgG glycosylation may be an important molecular mechanism in COVID-19.
- This [genetic study](#) in the United Kingdom applied Mendelian randomisation and colocalization approaches to understand the putative causal effects of 16,059 transcripts and 1,608 proteins on COVID-19 severity in European and effects of 610 proteins on COVID-19 severity in African ancestry. The authors identified one protein, SERPINA1, that showed effects on COVID-19 in African ancestry (OR=0.369,  $p = 9.96 \times 10^{-4}$ ), but weaker in European ancestry (OR=1.021,  $p = 0.745$ ). This implies that increased SERPINA1 levels may reduce COVID-19 risk in Africans. In addition, they identified four additional protein targets, FCRL3, ICAM5, ENTPD5 and OAS1, that showed effect on COVID-19 severity in Europeans. FCRL3, ICAM5 and ENTPD5 showed weaker effects in African ancestry, where OAS1 had no reliable genetic predictors in Africans. One protein ICAM1 showed suggestive effect in both ancestries, where alternative splicing may be a mediator linking ICAM1 with COVID-19 severity. This study provides a first step towards clinical investigation of beneficial and adverse effects of COVID-19 drug targets.

## Vaccines

- This [modelling study](#) assessed the global impact of the first year of COVID-19 vaccination programmes. A mathematical model of COVID-19 transmission and vaccination was separately fit to reported COVID-19 mortality and all-cause excess mortality in 185 countries and territories. Vaccinations prevented 14.4 million (95% CI, 13.7 to 15.9) deaths from COVID-19 between December 2020 and December 2021. This estimate rose to 19.8 million (95% CI, 19.1 to 20.4) deaths from COVID-19 averted when the authors used excess deaths as an estimate of the true extent of the pandemic, representing a global reduction of 63% in total deaths (19.8 million of 31.4 million) during the first year of COVID-19 vaccination. In COVAX Advance Market Commitment countries, they estimated that 41% of excess mortality (7.4 million [95% CI, 6.8 to 7.7] of 17.9 million deaths) was averted. In low-income countries, they estimated that an additional 45% (95% CI, 42 to 49) of deaths could have been averted had the 20% vaccination coverage target set by COVAX been met by each country, and that an additional 111% (95% CI, 105–118) of deaths could have been averted had the 40% target set by WHO been met by each country by the end of 2021. Inadequate access to vaccines in low-income countries has limited the impact in these settings, reinforcing the need for global vaccine equity and coverage.
- This [retrospective cohort study](#) in Italy assessed the vaccine effectiveness of BNT162b2 against SARS-CoV-2 infection and severe COVID-19 in children aged 5-11 years. The study involved 2,965,918 children who were followed up from 17 January to 13 April 2022. By the end of the follow-up period, 1,063,035 (35.8%) of the children had received two doses of the vaccine, 134,386 (4.5%) children had received one dose only, and 1,768,497 (59.6%) were unvaccinated. During the study period, 766,756 cases of SARS-CoV-2 infection and 644 cases of severe COVID-19 (627 hospitalisations, 15 admissions to intensive care units, and two deaths) were notified. Overall, vaccine effectiveness in the fully vaccinated group was 29.4% (95% CI 28.5–30.2) against SARS-CoV-2 infection and 41.1% (22.2–55.4) against severe COVID-19, whereas vaccine effectiveness in the partly vaccinated group was 27.4% (26.4–28.4) against SARS-CoV-2 infection and 38.1% (20.9–51.5) against severe COVID-19.



Vaccine effectiveness against infection peaked at 38.7% (37.7–39.7) at 0–14 days after full vaccination and decreased to 21.2% (19.7–22.7) at 43–84 days after full vaccination.

- This [population-based cohort study](#) in Canada assessed rates of reported myocarditis or pericarditis following receipt of a COVID-19 mRNA vaccine by product, age, sex, dose number, and inter-dose interval. The study involved 297 individuals who were reported to have myocarditis or pericarditis among 19,740,741 doses of mRNA vaccines administered. The authors found higher rates of myocarditis or pericarditis associated with receipt of mRNA-1273 (299.5 cases/1,000,000 doses; 95% CI, 171.2-486.4 cases/1,000,000 doses) compared with BNT162b2 (59.2 cases/1,000,000 doses (95% CI, 19.2-138.1 cases/1,000,000 doses) as a second dose, particularly among male individuals aged 18 to 24 years. Higher rates were also observed with shorter ( $\leq 30$  days) inter-dose intervals (BNT162b2: 52.1 cases/1,000,000 doses [95% CI, 31.8-80.5 cases/1,000,000 doses]; mRNA-1273: 83.9 cases/1,000,000 doses [95% CI, 47.0-138.4 cases/1,000,000 doses]) compared with  $\geq 56$  days (BNT162b2: 9.6 cases/1,000,000 doses [95% CI, 6.5-13.6 cases/1,000,000 doses]; mRNA-1273: 16.2 cases/1,000,000 doses [95% CI, 10.2-24.6 cases/1,000,000 doses]).
- This [observational cohort study](#) in Italy assessed the association between BNT162b2 vaccination and prevalence of long COVID. The study involved 2,560 health care workers with mild COVID in 9 health facilities from March 2020 to April 2022. Of 2,560 participants, 739 individuals (29%) had COVID-19 (89 asymptomatic), of whom 229 (31.0%; 95% CI, 27.7%-34.5%) had long COVID. The prevalence of long COVID varied across the pandemic waves, from 48.1% (95% CI, 39.9%-56.2%) in wave 1 to 35.9% (95% CI, 30.5%-41.6%) in wave 2 to 16.5% (95% CI, 12.4%-21.4%) in wave 3. The number of vaccine doses was associated with lower long COVID prevalence: 41.8% (95% CI, 37.0%-46.7%) in unvaccinated patients, 30.0% (95% CI, 6.7%-65.2%) with 1 dose, 17.4% (95% CI, 7.8%-31.4%) with 2 doses, and 16.0% (95% CI, 11.8%-21.0%) with 3 doses. Compared to unvaccinated females in wave 1 with no allergies or comorbidities, male sex (odds ratio [OR], 0.65; 95% CI, 0.44-0.98,  $P = .04$ ), 2 vaccine doses (OR, 0.25; 95% CI, 0.07-0.87,  $p = .03$ ), and 3 vaccine doses (OR, 0.16; 95% CI, 0.03-0.84,  $p = .03$ ) were associated with a lower probability of long COVID. Older age (OR, 1.23; 95% CI, 1.01-1.49,  $p = .04$ ), allergies (OR, 1.50; 95% CI, 1.06-2.11,  $p = .02$ ), and an increasing number of comorbidities (OR, 1.32; 95% CI, 1.04-1.68,  $p = .03$ ) were associated with a higher probability.
- This [population-based cohort study](#) in England assessed the association between body mass index (BMI) and COVID-19 vaccine uptake, vaccine effectiveness, and risk of severe COVID-19 outcomes after vaccination. The study involved 9,171,524 adults ( $\geq 18$  years) between December 2020 and November 2021. Among them, 566,461 tested positive for SARS-CoV-2 during follow-up, of whom 32,808 were admitted to hospital and 14,389 died. Of the total study sample, 19.2% (1,758,689) were unvaccinated, 3.1% (287,246) had one vaccine dose, 52.6% (4,828,327) had two doses, and 25.0% (2,297,262) had three doses. In people aged 40 years and older, uptake of two or three vaccine doses was more than 80% among people with overweight or obesity, which was slightly lower in people with underweight (70–83%). Protection against severe COVID-19 disease (comparing people who were vaccinated vs those who were not) was high after 14 days or more from the second dose for hospital admission (underweight: OR 0.51 [95% CI 0.41–0.63]; healthy weight: 0.34 [0.32–0.36]; overweight: 0.32 [0.30–0.34]; and obesity: 0.32 [0.30–0.34]) and death (underweight: 0.60 [0.36–0.98]; healthy weight: 0.39 [0.33–0.47]; overweight: 0.30 [0.25–0.35]; and obesity: 0.26 [0.22–0.30]). These results suggest the need for targeted efforts to increase uptake in people with low BMI ( $< 18.5$  kg/m<sup>2</sup>), in whom uptake is lower and vaccine effectiveness seems to be reduced.

## Diagnostics

- This [prospective cohort study](#) in the United Kingdom evaluated daily lateral flow testing (LFT) as an alternative to 10-14 days quarantine for key worker contacts of known COVID-19 cases. The study involved 1,657 participants from Police, Fire and Rescue service and Children's Hospital. Compliance with the daily testing regime was 96.9%, 93.7% and 92.8% across the three main organisations respectively. There were 34 positive COVID-19 cases identified, 3 of which were undetected by the daily LFT regime. A total of 8,291 workdays would have been lost to self-isolation but were prevented

due to negative daily tests. Organisations reported that daily contact testing proved useful, flexible and well-tolerated initiative to sustain key worker services.

- This [cohort study](#) in the United Kingdom assessed SARS-CoV-2-specific T cell responses in patients with confirmed SARS-CoV-2 infection and/or Long COVID. The authors performed highly sensitive fluorospot assays on peripheral blood mononuclear cells from 72 patients who attended the Long COVID clinic at Cambridge University Hospital. Interleukin-2 (IL-2) release (but not Interferon release) from T cells in response to SARS-CoV-2 peptides is both sensitive (75% +/-13%) and specific (88% +/-7%) for previous SARS-CoV-2 infection >6 months after a positive PCR test. They identified that 42–53% of patients with Long COVID, but without detectable SARS-CoV-2 antibodies, nonetheless have detectable SARS-CoV-2 specific T cell responses. These results demonstrate that T cell assays are a sensitive and effective method to determine past SARS-CoV-2 infection. This could benefit patients with Long COVID by confirming their belief that they had COVID-19 and allow clinicians to diagnose Long COVID based on symptom profile and evidence of past infection.
- This [study](#) in Tunisia describes the development of a quantitative in-house ELISA to compare the efficiency of different COVID-19 vaccines used in the National Vaccination Program. The ELISA is based on the ectodomain of the SARS-CoV-2 Spike Baculovirus recombinant protein. The authors used a panel of 145 COVID-19 RT-PCR positive serum samples and 116 pre-pandemic serum samples as a negative panel. The validation was carried out by comparison to four commercial techniques (Vidas SARS-CoV-2 IgG anti-RBD Biomérieux, Elecsys Anti-Nucleocapsid of SARS-CoV-2 Roche, cPass GenScript and the quantitative Elecsys Anti-RBD of SARS-CoV-2, Roche). For the evaluation of the National Vaccination campaign, they included 115 recipients who received one of the approved vaccines. The qualitative performances of the developed ELISA gave 96% sensitivity, 97.5% specificity and 0.968 accuracy. For the evaluation of the different brand of vaccines in recipients not previously infected with SARS-CoV-2, the mRNA vaccine of Pfizer/BioNTech showed a higher efficacy compared to inactivated virus vaccines.
- This [study](#) in Denmark describes the development and performance of a device (AeroCollect) designed to detect SARS-CoV-2 in exhaled breath from humans. The study involved obtaining 665 air samples from 111 participants with confirmed SARS-CoV-2 infection by RT-PCR. Overall, 52 individuals (46.8%) had at least one positive air sample and 129 (19.4%) air samples were positive for SARS-CoV-2. Participants with symptoms or a symptom duration ≤ four days had significantly higher odds of having a positive air sample. Cycle threshold values were significantly lower in samples obtained ≤ 4 days from symptom onset. Neither variant of SARS-CoV-2 nor method of air sampling were associated with a positive air sample. These results demonstrate that SARS-CoV-2 is detectable in human breath by electrostatic air sampling with the highest detection rate closest to symptom onset. The authors recommend further evaluation of the air sampling technique to increase sensitivity.

## Care and Treatment

- This [cross-sectional study](#) in the United States assessed the association between SARS-CoV-2 variants and proportion of children with croup, as well as hospital and intensive care unit (ICU) admissions and racemic epinephrine (RE) treatment. The study included 5,152 children (aged 3 months to 8 years) with COVID-19 related croup across 43 children's hospitals from January 2021 to March 2022. Proportion of children with COVID-19-related croup was significantly increased during Omicron (10.9%) compared with Alpha or other variant (4.1%) and Delta (3.6%) periods ( $p < .001$ ). Odds of hospitalisation during Alpha or other variant (adjusted odds ratio [aOR], 1.28; 95% CI, 0.97-1.70) or Delta (aOR, 0.92; 95% CI, 0.74-1.15) periods were not significantly different compared with the period of Omicron predominance. Treatment with RE was less likely during the Delta period (aOR, 0.73; 95% CI, 0.61-0.87) and did not differ in the Alpha or other variant periods (aOR, 1.03; 95% CI, 0.81-1.31) compared with the period of Omicron predominance. The frequency of ICU admission was not statistically different across time periods. These findings suggest that paediatric health systems should consider variation in SARS-CoV-2 phenotypes and their association with patient care.
- This [retrospective cohort study](#) of individuals with mild COVID-19 during different SARS-CoV-2 variant waves in Brazil assessed the prevalence of self-reported olfactory dysfunction. The study involved

6,053 participants from March 2020 to March 2022. Olfactory dysfunction was reported by 2,650 participants. Olfactory dysfunction was reported by 2,223 of the 4,227 participants (52.6% [95% CI, 51.1%-54.1%]) diagnosed during the period of the original lineages. The prevalence decreased to 27.5% (95% CI, 24.3%-30.8%) during Gamma, 42.1% (95% CI, 37.4%-47.0%) during Delta, and 5.8% (95% CI, 4.4%-8.5%) during Omicron. The odds of olfactory dysfunction were lower for those infected during Gamma (adjusted odds ratio [aOR], 0.48 [95% CI, 0.39-0.59]) and Omicron (aOR, 0.07 [95% CI, 0.05-0.10]) compared with the original lineages period. No association was observed during Delta (aOR, 0.90 [95% CI, 0.71-1.15]). The sensitivity analysis found an adjusted OR of 0.09 (95% CI, 0.06-0.15) for olfactory dysfunction during Omicron vs Gamma after additional adjustment for vaccination status. These results suggest that the type of SARS-CoV-2 variant might be a risk factor for olfactory dysfunction.

- This [open-label, multicentre, randomised, controlled, phase 3b trial](#) evaluated the efficacy and safety of prophylactic low-molecular-weight heparin (enoxaparin) versus standard of care (no enoxaparin) in at-risk outpatients with COVID-19. The study involved 219 participants across 15 sites in 6 countries (Belgium, Brazil, India, South Africa, Spain, and the UK). There was no difference in the composite of all-cause mortality and hospitalisation at 21 days between the enoxaparin group (12 [11%] of 105 patients) and the standard-of-care group (12 [11%] of 114 patients; unadjusted hazard ratio 1.09 [95% CI 0.49–2.43]; log-rank  $p=0.83$ ). At 21 days, two (2%) of 105 patients in the enoxaparin group (one minor bleed and one bleed of unknown severity) and one (1%) of 114 patients in the standard-of-care group (major abnormal uterine bleeding) had a bleeding event. Adverse events were reported from 22 (21%) patients in the enoxaparin group and 13 (11%) patients in the standard-of-care group. The most common adverse event in both groups was COVID-19-related pneumonia (6 [6%] patients in the enoxaparin group and 5 [4%] patients in the standard-of-care group). These results suggest that prophylaxis with low-molecular-weight heparin had no benefit for at-risk outpatients with COVID-19.

## Epidemiology

- This [study](#) in the United States assessed whether the presence of sickle cell trait (SCT) was associated with worse outcomes of COVID-19. The study involved 132,577 participants from the Million Veteran Program (2729 persons with SCT and 129 848 who were SCT negative). Sickle cell trait was present in 7.8% of individuals of African ancestry and associated with a history of chronic kidney disease, diabetic kidney disease, hypertensive kidney disease, pulmonary embolism, and cerebrovascular disease. SCT was associated with an increased COVID-19 mortality in individuals of African ancestry ( $n = 3749$ ; odds ratio, 1.77; 95% CI, 1.13 to 2.77;  $p = .01$ ). In the 60 days following COVID-19, SCT was associated with an increased incidence of acute kidney failure. A counterfactual mediation framework estimated that on average, 20.7% (95% CI, -3.8% to 56.0%) of the total effect of SCT on COVID-19 fatalities was due to acute kidney failure.
- This [prospective, community-based paediatric cohort study](#) in Nicaragua characterised the burden of COVID-19 and assessed how risk of symptomatic reinfection varied by age among children. The study involved 1,964 children aged 0 to 14 years in District 2 of Managua from 1 March 2020 to 15 October 2021. Of 1824 children who were tested, 908 (49.8%; 95% CI, 47.5%-52.1%) were seropositive during the study. There were also 207 PCR-confirmed COVID-19 cases, 12 (5.8%) of which were severe enough to require hospitalisation. Incidence of COVID-19 was highest among children younger than 2 years (16.1 cases per 100 person-years; 95% CI, 12.5-20.5 cases per 100 person-years), which was approximately 3 times the incidence rate in any other child age group assessed. In addition, 41 symptomatic SARS-CoV-2 episodes (19.8%; 95% CI, 14.4%-25.2%) were reinfections. These findings suggest that the burden of COVID-19 and associated severe illness may not be evenly distributed across age groups in children.
- This [nationwide population-based cohort study in France](#) assessed associations between the residual risk of COVID-19 hospitalisation or in-hospital death despite vaccination and 47 chronic conditions by July 2021. The study involved 28,031,641 fully vaccinated individuals with an average follow-up of 80 days. A total of 5,345 participants (87 hospitalisations per 100,000 person-years) were hospitalised for COVID-19 and 996 (16 in-hospital death per 100,000 person-years) died in hospital. A higher risk was



observed with increasing age, male gender, and social deprivation. Most of the 47 chronic conditions considered were positively associated with an increased risk of COVID-19-related hospitalisation and a slight excess risk of death. The risk of hospitalisation and In-hospital death for COVID-19 also increased with the use of immunosuppressants (aHR 3.3 [2.8-3.8] and 2.4 [1.7-3.5], respectively) and oral corticosteroids (aHR 2.8 [2.5-3.1] and 4.1 [3.3-5.1]). There was a strong association between an increasing number of comorbidities and the risk of hospitalisation and in-hospital death (e.g., 5+ versus none, aHR 10.1 95%CI 9.0-11.5 and 17.8 95%CI 11.5-27.4, respectively). These findings highlight the remaining residual risk concentrated among the elderly, immunocompromised, and poly pathological populations that require complementary preventive measures.

- This [nationwide cohort study](#) in Denmark compared SARS-CoV-2 infection rates before and after a primary infection among still unvaccinated individuals, adjusting for sex, age, comorbidity and residency. The authors analysed register data since the beginning of the pandemic until March 2022. Their results revealed a consistently high protection of 83.4% (95%CI: 82.2–84.6%) from reinfection for the Wuhan, and Alpha variants, increasing to 88.3% (95%CI: 85.9–90.3%) when estimated among symptomatic infections. However, protection diminished with time when Delta appeared and with the emergence of the Omicron variant in Denmark, the level of protection offered by previous infection with other variants was estimated at 51% (95%CI: 50.1–52.0%) after three months, declining to 25% after six months between the two infections. The protective effect was lower in elderly people but generally higher following a first symptomatic as opposed to asymptomatic infection.

### Infection Prevention & Control

- This [cross-sectional study](#) in Nigeria assessed the magnitude and determinants of vaccine hesitancy among health workers (HWs). The study involved 10,184 HWs across all states between March and April 2021. A total of 9,369 HWs [92% (95% CI= 91, 92)] were confident of the COVID-19 vaccines and were already vaccinated at the time of the survey. Compared to HWs who were less than 20 years old, those aged 50 – 59 years were significantly more confident of the COVID-19 vaccines and had been vaccinated (OR=3.8, 95% CI=2.3 – 6.4,  $p < 0.001$ ). Only 858 (8%) of the HWs interviewed reported being hesitant with 57% (479/858) having received negative information, with the commonest source of information from social media (43.4%). The issues identified remain a significant risk to the success of subsequent phases of the vaccine rollout in Nigeria.

### Non-pharmaceutical interventions, social distancing

- This [cohort study](#) in France assessed changes in invasive pneumococcal disease (IPD) incidence after the implementation of NPIs during the COVID-19 pandemic. The authors also assessed the temporal association with changes in pneumococcal carriage rate and respiratory viral infections (specifically respiratory syncytial virus [RSV] and influenza cases) among children. The study involved 11,944 children <15 years from a national continuous surveillance system between January 2007 and March 2021. After NPI implementation, IPD incidence decreased by 63% (95% CI, –82% to –43%;  $p < .001$ ) and was similar for non–13-valent pneumococcal conjugate vaccine serotypes with both high disease potential (–63%; 95% CI, –77% to –48%;  $p < .001$ ) and low disease potential (–53%; 95% CI, –70% to –35%;  $p < .001$ ). The overall pneumococcal carriage rate did not significantly change after NPI implementation nor did the carriage rate for non-PCV13 serotypes with high disease potential or low disease potential. After NPI implementation, the estimated number of influenza cases decreased by 91% (95% CI, –74% to –97%;  $p < .001$ ), and the estimated number of RSV cases decreased by 74% (95% CI, –55% to –85%;  $p < .001$ ). Overall, the decrease in influenza and RSV cases accounted for 53% (95% CI, –28% to –78%;  $p < .001$ ) and 40% (95% CI, –15% to –65%;  $p = .002$ ) of the decrease in IPD incidence during the NPI period, respectively. The decrease in IPD incidence was not associated with pneumococcal carriage, with carriage accounting for only 4% (95% CI, –7% to 15%;  $p = .49$ ) of the decrease.



## D. Clinical Trials Updates

### Key updates:

#### Vaccine trials:

- On 5 July 2022, [Novavax announced the European Commission \(EC\) has approved the expanded conditional marketing authorization \(CMA\) of Nuvaxovid \(NVX-CoV2373\) COVID-19 vaccine in the European Union \(EU\) for adolescents aged 12 through 17.](#) The approval follows the positive recommendation made by the European Medicines Agency's Committee for Medicinal Products for Human Use. The authorization was 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. Preliminary safety data from the trial 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 29 June 2022, [Seattle biotech HDT Bio Corp reported Indian regulators have issued an Emergency Use Approval for Gemcovac, a ground-breaking COVID-19 vaccine which uses self-amplifying RNA \(or "saRNA"\) to replicates itself following administration and is thus effective at extremely low doses.](#) In addition, it is stable at refrigerator temperatures and currently is undergoing clinical trials in the U.S., Brazil, and South Korea.
- On 28 June 2022, [EnGeneIC Biopharma is currently conducting trials of its ground-breaking vaccine in Sydney and Melbourne which offer immunity against all variants.](#) The vaccine utilize platform technology based around a biological nanocell (EDV; EnGeneIC Dream Vector). Initially developed as a breakthrough in cancer treatment, these EDVs are loaded with anti-viral molecules to deliver a world first nano-cellular COVID-19 vaccine. Clinical trials have shown the novel vaccine works by stimulating a completely different immune pathway from other vaccines, producing "high affinity" antibodies that neutralise all COVID-19 variants. Thirty-two healthy participants received two doses, three weeks apart. Of those, 27 have passed the 28-day safety assessment with no side effects. Critically, they all have high affinity antibodies capable of neutralising all COVID-19 mutants, including Omicron.
- On 26 June 2022, [European Medicines Agency \(EMA\) recommended granting a marketing authorisation for COVID-19 Vaccine \(inactivated, adjuvanted\) Valneva for use in the primary vaccination of people from 18 to 50 years of age.](#) COVID-19 Vaccine (inactivated, adjuvanted) Valneva contains inactivated (killed) whole particles of the original strain of SARS-CoV-2 that cannot cause disease. After a thorough evaluation, EMA's human medicines committee (CHMP) concluded by consensus that the data on the vaccine were robust and met the EU criteria for efficacy, safety and quality. The main study conducted with Valneva's vaccine is an immunobridging trial. Immunobridging trials compare the immune response induced by a new vaccine with that induced by an authorised comparator vaccine proven to be effective against the disease. Results from the study, which involved nearly 3,000 people aged 30 years and older, showed that the vaccine triggers the production of higher levels of antibodies against the original strain of SARS-CoV-2 than the comparator, Vaxzevria. In addition, the proportion of people who produced a high level of antibodies was similar for both vaccines. Additional data from same study showed the vaccine is as effective at triggering the production of antibodies in people aged between 18 and 29 as it is in people aged 30 years and older. Clinical trial registration #: (NCT04671017).
- On 25 June 2022, [Pfizer and BioNTech SE today announced positive data evaluating the safety, tolerability, and immunogenicity of two Omicron-adapted COVID-19 vaccine candidates: one monovalent and the other bivalent, a combination of the Pfizer-BioNTech COVID-19 Vaccine and a vaccine candidate targeting the spike protein of the Omicron BA.1 variant of concern.](#) The Omicron adapted vaccine candidates (30 µg and 60 µg) studied in 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 Pfizer current COVID-19 vaccine. The pre-specified criterion for superiority was measured by the ratio of neutralising geometric mean titres (GMR) with the lower bound of the 95% confidence interval >1. 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 24 June 2022, [Sanofi and GSK announced positive data from their vaccine trial which evaluated an adjuvanted bivalent D614 and Beta \(B.1.351\) vaccine candidate](#). The vaccine is the first candidate to demonstrate efficacy in a placebo-controlled trial in an environment of high Omicron variant circulation. In Stage 2 of the Phase 3 COVID-19 vaccine trial VAT08 of more than 13,000 participants 18 and above years of age, the Beta-containing vaccine candidate demonstrated an efficacy of 64.7% (95% confidence interval [CI, 46.6, 77.2]) against symptomatic COVID-19 and 72% efficacy (95% confidence interval [CI, 45.8, 86.6]) in Omicron-confirmed symptomatic cases. In previously seropositive populations, the vaccine candidate demonstrates an overall efficacy of 75.1% (95% confidence interval [CI, 56.3, 86.6]) against symptomatic infection, and 93.2% (95% confidence interval [CI, 73.2, 99.2]) in Omicron-confirmed symptomatic cases. Throughout Stage 1 and Stage 2 of the VAT08 trial (~23,000 participants in total), the vaccine demonstrated a favourable safety and tolerability profile. Clinical trial registration #: (NCT05124171).
- On 23 June 2022, [Novavax announced that the Nuvaxovid \(NVX-CoV2373\) COVID-19 vaccine has been recommended for expanded conditional marketing authorization \(CMA\) in the European Union \(EU\) for adolescents aged 12 through 17](#). The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency based its opinion on results from the Phase 3 PREVENT-19 clinical trial. The CHMP recommendation was based on data from the ongoing paediatric expansion of PREVENT-19, a pivotal Phase 3 trial of 2,247 adolescents aged 12 through 17 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. Preliminary safety data from the trial 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. Local and systemic reactogenicity was generally lower than or similar to adults, after the first and second dose. The most common adverse reactions observed were injection site tenderness/pain, headache, myalgia, fatigue, and malaise. Clinical trial registration #: (NCT04611802).
- On 23 June 2022, [Novavax announced the Taiwan Food and Drug Administration has granted emergency use authorization \(EUA\) for Nuvaxovid \(NVX-CoV2373\) COVID-19 vaccine in individuals aged 18 years and over](#). The EUA was based on the totality of preclinical, manufacturing, and clinical trial data submitted for review which includes two pivotal Phase 3 clinical trials: PREVENT-19. These trials enrolled approximately 45,000 participants aged 18 years and older in the U.S., Mexico, and a UK. In both trials, the vaccine demonstrated efficacy with a reassuring safety and tolerability profile. Clinical trial registration #: (NCT04611802).
- On 22 June 2022, [Moderna announced new clinical data on its bivalent \(Omicron\) COVID-19 booster candidate, mRNA-1273.214](#). One month after administration in previously vaccinated and boosted participants, a 50 µg booster dose of mRNA-1273.214 elicited potent neutralising antibody responses against the Omicron subvariants BA.4 and BA.5 in all participants regardless of prior infection. Data shows, mRNA-1273.214 boosted neutralising titres against BA.4/BA.5 by 5.4-fold (95% CI: 5.0, 5.9) above baseline in all participants regardless of prior infection, and by 6.3-fold (95% CI: 5.7, 6.9) in the subset of seronegative participants. Neutralising titres against BA.4/BA.5 were approximately 3-fold lower than previously reported neutralising titres against BA.1. One month after an mRNA-1273.214 booster, neutralising geometric mean titres (GMT) against BA.4/BA.5 were 941 (95% CI: 826, 1071) in all participants, and 727 (95% CI: 633, 836) in seronegative participants. For context, prior studies of a third dose of the prototype booster induced neutralising GMT against BA.1 of 629 (95% CI: 526, 751) and against Delta of 828 (95% CI: 738, 928). A third dose of the prototype booster was shown to be effective against Delta and BA.1 infection and hospitalisation in observational studies. The ongoing

Phase 2/3 study with approximately 800 participants demonstrated a 50µg booster dose of mRNA-1273.214 met all pre-specified primary endpoints, including superiority in neutralising antibody GMT against Omicron (BA.1) when compared to a 50µg booster dose of the prototype booster (mRNA-1273). The bivalent booster was generally well tolerated, with a reactogenicity and safety profile that was consistent with the prototype booster. Clinical trial registration #: (NCT05249829).

#### Therapeutics trials:

- On 30 June 2022, [Pfizer announced the submission of a New Drug Application \(NDA\) to the U.S. Food and Drug Administration \(FDA\) for approval of PAXLOVID \(nirmatrelvir \[PF-07321332\] tablets and ritonavir tablets\) for patients who are at high risk for progression to severe illness from COVID-19. The submission is supported by non-clinical and clinical data for PAXLOVID.](#) It includes results from the Phase 2/3 EPIC-HR study (Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients), which found that, compared to placebo, treatment with PAXLOVID reduced the risk of hospitalisation or death from any cause by 88% in non-hospitalised, high-risk adult patients treated within five days of symptom onset; results from the final Clinical Study Report showed an 86% reduction in relative risk. It also comprised of the most recent analyses which included data from both vaccinated patients with, and unvaccinated patients without, risk factors for severe COVID-19. While the novel primary endpoint of self-reported, sustained alleviation of all symptoms for four consecutive days was not met, the data were supportive of the efficacy and safety observed for use in patients at increased risk of progression to severe COVID-19 illness. Clinical trial registration #: (NCT04381936).
- On 27 June 2022, [Rensselaer Polytechnic Institute reported to receive grant from the National Institute of Allergy and Infectious Diseases \(NIAID\), part of the National Institutes of Health \(NIH\), to develop a low-dose, oral COVID antiviral drug that can be administered at home.](#) They will build on the previous research findings published in Cell Reports, which shows that out of the 10 hepatitis C drugs tested, seven suppressed the SARS-CoV-2 virus. Three of those drugs were acting not only on the main protease, CLpro, but on the PLpro protease, as well. When combined with the polymerase inhibitor remdesivir, these drugs multiplied remdesivir's antiviral activity by as much as tenfold. Those that only inhibit CLpro did not amplify remdesivir's effect. The Institute will work towards making new and orally bioavailable PLpro inhibitors, looking at the structure of the protein's active site and design molecules that fit into it and bind with optimal affinity.
- On 23 June 2022, [Altamira announced that it has reached its targeted enrolment of 136 confirmed subjects in its COVAMID clinical investigation to evaluate the safety, tolerability, and efficacy of its Bentrion nasal spray in patients with acute COVID-19.](#) Bentrion is a drug-free nasal spray for personal protection against airborne viruses and allergens. Upon application into the nose, Bentrion forms a protective gel layer on the nasal mucosa. This thin film is designed to prevent the contact of viruses or allergens with cells. COVAMID is a randomised, placebo controlled clinical trial to evaluate the ability of Bentrion nasal spray to reduce the SARS-CoV-2 viral load in the nose, alleviate COVID-19 signs and symptoms, and decrease the frequency of COVID-19 related hospital admissions. In the COVAMID trial, the COVID-19 patients are randomised at a 2:1:1 ratio to receive for 10 days either Bentrion, a placebo (Bentrion minus its key mineral component), or no treatment, followed by a 10-day observation phase. It is being conducted in Bulgaria and North Macedonia. Having reached the target enrolment and following completion of data entry and verification, a pre-specified blinded interim analysis will determine whether the initial assumptions for the statistical powering of the study have been met.
- On 22 June 2022, [The University of New Hampshire researchers found that using an already existing drug compound in a new way, known as drug repurposing, could be successful in blocking the activity of a key enzyme of the coronavirus, or SARS-CoV-2, which causes COVID-19.](#) It works through utilisation of strategic therapeutic that could possibly disrupt key steps in the viral life cycle at the molecular level, like the first contact with a healthy cell or the first step in replicating within an infected cell. Structure, Function, and Bioinformatics, researchers set out to target a key enzyme responsible for COVID-19, called the main protease enzyme Mpro, which has become a primary target of intense research and therapeutic development because it is essential for the virus to replicate. In this case, they explored the inhibiting properties of a derivative of the potent chemical compound known as Thiadiazolidinones, or TDZD, which are already being studied as a potential treatment for neurological

disorders like Parkinson's Disease. Researchers used a specific TDZD compound, known as CCG-50014, to target Mpro which acts like a molecular scissor by cutting up long chains of polypeptide proteins of the virus into smaller component proteins. These smaller segments can fold and mature to form new virus particles. Using molecular dynamics simulations combined with laboratory experiments, the researchers determined that TDZD compound was able to inhibit the Mpro enzyme.

Immunotherapies trials:

- None

### Contributors

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