COVID-19 Scientific and Public Health Policy Update¹
(3 August 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

<table>
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<tr>
<th>920 Million Vaccines Supplied</th>
<th>637 Million Vaccines Administered</th>
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<tr>
<td>22.5% Partially Vaccinated</td>
<td>20.3% Fully Vaccinated*</td>
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*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 3 August 2022

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

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

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

The Omicron variant (B.1.1.529), first reported in South Africa on 24th November 2021, has spread to 198 countries/territories/areas worldwide. As of 3 August 2022, 50 (90.9%) of the 55 Member States in Africa have reported this variant. For more information visit https://africacdc.org/institutes/africa-pathogen-genomics-initiative/.

Member States

- Reported Omicron Variant
- Omicron Variant not yet reported
- No available data for SARS-CoV-2 Sequence

Updated 3 August 2022

B. New guidelines and resources

Since 19 July 2022,

- Africa CDC\(^2\) has published new guidance and resources on:
  - Africa CDC – Mastercard Foundation: Saving Lives and Livelihoods Newsletter, July 2022
  - Outbreak Brief 132: Coronavirus Disease 2019 (COVID-19) Pandemic

- U.S. CDC\(^3\) has published new guidance and resources on:
  - Selected Adverse Events Reported after COVID-19 Vaccination

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\(^2\) Africa CDC: Africa Centres for Disease Control and Prevention
\(^3\) U.S. CDC: United States Centers for Disease Control and Prevention

Global Community Mitigation

WHO has published new guidance and resources on:

- Implementation guide for vaccination of health workers
- Global surveillance of COVID-19: WHO process for weekly reporting aggregated data
- Revised case report form for confirmed Novel Coronavirus COVID-19 (report to WHO within 48 hours of case identification)
- WHO COVID-19 Case definition
- Public health surveillance for COVID-19: interim guidance

U.S. FDA has issued press releases on:

- As of 2 August, 438 tests and sample collection devices are authorised by the FDA under emergency use authorisations (EUAs)

ECDC has issued new resources on:

- Methods for the detection and characterisation of SARS-CoV-2 variants - second update
- ECDC expert consultation on knowledge and research gaps related to the COVID-19 public health response

UKHSA has issued new guidance and press releases on:

- Ventilation to reduce the spread of respiratory infections, including COVID-19
- Preventing and controlling outbreaks of COVID-19 in prisons and places of detention
- COVID-19: testing in the workplace and eligible high-risk settings
- Using the NHS COVID Pass to demonstrate COVID-19 status

C. Scientific updates

Basic Science

This study in the United States combined genomic and epidemiological data from early in the COVID-19 pandemic with phylodynamic models and epidemic simulations to show that the pandemic most likely began with at least two separate zoonotic transmissions starting in November 2019. The first zoonotic transmission likely involved lineage B viruses around 18 November 2019 (23 October–8 December), while the separate introduction of lineage A likely occurred within weeks of this event. These findings indicate that it is unlikely that SARS-CoV-2 circulated widely in humans prior to November 2019 and define the narrow window between when SARS-CoV-2 first jumped into humans and when the first cases of COVID-19 were reported.

This study in the Netherlands identified and humanized a monoclonal antibody, 87G7, that retained potent in vitro neutralising activity against SARS-CoV-2 variants including the Alpha, Beta, Gamma, Delta, and Omicron (BA.1/BA.2) variants of concern (VOCs). The authors identified the specific interactions that the antibody has with the receptor binding domain (RBD) region of Omicron, showing that the antibody can overcome various RBD mutations. 87G7 protected mice and hamsters prophylactically against challenge with all current SARS-CoV-2 VOCs and showed therapeutic activity.
against SARS-CoV-2 challenge in both animal models. Their findings demonstrate that 87G7 holds promise as a prophylactic or therapeutic agent for COVID-19 that is more resilient to SARS-CoV-2 antigenic diversity.

- This review from China presents recent advances and future trends in the development of aptamer-based approaches for SARS-CoV-2 diagnosis and treatment. An aptamer is a single stranded DNA or RNA molecule, which can bind to targets by folding into a three-dimensional structure. Aptamers have been developed for the detection and inhibition of a number of different viruses, such as HIV, influenza viruses, MERS-CoV and SARS-CoV. Aptamers targeting SARS-CoV-2 represent a promising tool to fight against COVID-19, which is of paramount importance for the current and any future pandemics.

**Vaccines**

- This cohort study in the United States assessed the probability of SARS-CoV-2 reinfection and the effectiveness associated with vaccination after recovery from COVID-19. The study involved 95,000 participants aged 12 years and older who were previously diagnosed with COVID-19 and unvaccinated at the time of first infection, stratified into 3 subpopulations: long-term congregate care (LTCC) residents, LTCC employees, and the general population. Probability of reinfection at 9 months for those who remained unvaccinated after recovery from prior COVID-19 was 13.0% (95% CI, 12.0%-14.0%) among LTCC residents, 10.0% (95% CI, 8.8%-11.5%) among LTCC employees, and 1.9% (95% CI, 1.8%-2.0%) among the general population. Completion of the primary vaccination series after infection was associated with 49% (95% CI, 27%-65%) protection among LTCC residents, 47% (95% CI, 19%-65%) protection among LTCC employees, and 62% (95% CI, 56%-68%) protection in the general population against reinfection, adjusting for potential sociodemographic and clinical confounders and temporal variation in infection rates. These findings suggest that among people who have recovered from COVID-19, subsequent completion of the primary vaccination series reduced the risk of reinfection by approximately half.

- This case series in the United States present 6 patients who experienced skin reactions after mRNA-based vaccination against SARS-CoV-2. The cohort consisted of 3 males and 3 females. One patient had a history of psoriasis and transverse myelitis, and 1 had multiple sclerosis. All patients received the Pfizer/BioNTech COVID-19 mRNA vaccine. Median time between the first vaccine dose and lesion development was 22 days (range, 4-42 days). Two patients endorsed vaccine-related constitutional symptoms, and 3 reported lesionsal pruritus. Cutaneous eruptions were characterized by single (n = 2) or generalized (n = 4) papulonodules on the trunk and/or extremities. Histologic examination revealed T-cell–predominant lymphoid infiltrates consistent with pityriasis lichenoides et varioliformis acuta (n = 2), cutaneous T-cell lymphoid hyperplasia (CLH) (n = 2), and lymphomatoid papulosis type A (n = 2). The clinical course was indolent with resolution after various therapies. These findings raise awareness about low-grade cutaneous lymphoid reactions after COVID-19 vaccination.

- This randomised clinical trial in the United States assessed whether behavioural nudges delivered through text messages could accelerate adherence to a health system’s COVID-19 vaccination policy. The study included 2000 participants who were randomly assigned (1:1) to control or to receive a text message intervention that stated a vaccine had been reserved for the participant, with a scheduled date for vaccination within a 2-week period. By the end of the 2-week intervention, 363 participants in the text message nudge group (36.3%) and 318 participants in the control group (31.8%) were adherent with the vaccination policy, representing a significant increase of 4.9 (95% CI, 0.8 to 9.1) percentage points in adjusted analyses comparing the nudge group with the control group (p = 0.02). Among participants who became adherent by the end of the 4-week follow-up period, the text message nudge significantly reduced time to adherence by a mean of 2.4 (95% CI, 2.1 to 4.7) days (p < 0.001) and a median of 5.0 (95% CI, 2.5 to 7.7) days (p < 0.001) compared with the control group. At 4 weeks, overall vaccination adherence was no longer different between groups (control: 477 participants [47.7%]; intervention: 472 participants [47.2%]).

- This multicentre, randomised, single-blind trial in France assessed the immunogenicity and safety of two adjuvanted recombinant vaccines and the messenger RNA vaccine BNT162b2 administered as a booster. The study involved 223 participants who had received 2 doses of BNT162b2, participants were
assigned (1:1:1) to receive booster vaccination with one of the following: a third dose of BNT162b2, a dose of the Sanofi–GSK SARS-CoV-2 adjuvanted recombinant protein MVB.1.351 vaccine, or a dose of the SARS-CoV-2 adjuvanted recombinant protein MVB.1.351 vaccine. The percentage of participants who had an increase in the neutralising-antibody titer by a factor of at least 10 between day 0 and day 15 for the original strain was 55% (95% CI, 43 to 67) in the MVD614 group, 76% (95% CI, 64 to 85) in the MVB.1.351 group, and 63% (95% CI, 51 to 74) in the BNT162b2 group. For the beta variant, the corresponding percentages were 45% (95% CI, 33 to 57), 85% (95% CI, 74 to 92), and 51% (95% CI, 40 to 63). The MVB.1.351 vaccine elicited higher neutralising-antibody titres than the other vaccines against the original strain and against the beta, delta, and omicron BA.1 variants. The use of new vaccines that contain beta spike protein may be an interesting strategy for broader protection against SARS-CoV-2 variants.

• This mouse model study in the United Kingdom tested whether antibodies targeting the more conserved S2 subunit of the spike protein could confer protection against infection with distinct coronaviruses. The authors observed that S2-targeted vaccination produced antibodies that could neutralise diverse alpha-coronaviruses and beta-coronaviruses. These antibodies had increased breadth relative to antibodies elicited by full-length spike protein vaccination, suggesting less repertoire focusing. Their findings establish the protective value of an S2-targeting vaccine and support the notion that S2 vaccination may better prepare the immune system to respond to the changing nature of the S1 subunit in SARS-CoV-2 variants of concern, as well as to future coronavirus zoonoses.

• This cross-sectional in China assessed the risk of gout flares in the first 3 months after COVID-19 vaccination with inactivated virus, and whether colchicine can prevent gout flares following post-COVID-19 vaccination. The study enrolled 549 gout patients (median age 39 years, 84.2% vaccinated). For the 462 patients who received COVID-19 vaccine, 203 (43.9%) developed at least one gout flare in the 3 months after vaccination. Most of the flares were experienced within 1 month after the first (99/119 (83.2%)) or second (70/115 (60.9%)) dose of vaccine. Compared with unvaccinated participants, COVID-19 vaccination was associated with higher odds of gout flare within 3 months (adjusted OR 6.02; 95% CI 3.00 to 12.08). Colchicine use was associated with 47% less likelihood of postvaccine gout flare. These findings may inform discussions with patients with gout about the risks of gout flare around the time of COVID-19 vaccination.

Diagnostics

• This study in Canada describes the development & performance of an impedance-based affinity biosensor using Interdigitated Electrode (IDE) arrays to detect antibodies to SARS-CoV-2 in serum. The authors created the biosensor by functionalizing the IDEs’ surface with abacalovirus-expressed and purified Spike (S) protein to bind anti-SARS CoV-2 antibodies. Gold nanoparticles (GNP) fused to protein G were used to probe for bound antibodies. An ELISA assay using horseradish peroxidase-protein G to probe for bound IgG confirmed that the purified S protein bound a commercial source of anti-SARS-CoV-2 antibodies specifically and bound anti-SARS-CoV-2 antibodies in COVID-19 positive serum. The biosensor could detect anti-SARS-CoV-2 antibodies with 72% sensitivity in 2 hours. Using GNP-protein G, the affinity biosensor had increased impedance changes with COVID-19 positive serum and minimal or decreased impedance changes with negative serum.

• This study in Italy assessed the sensitivity and specificity of the Idylla SARS-CoV-2 Test, a fully automated RT-PCR platform (Biocartis NV, Mechelen, Belgium), using samples from previously tested SARS-CoV-2 suspects by conventional RT-PCR. The authors retrieved 55 nasopharyngeal swabs from symptomatic patients or from people who have been in close contact with COVID-19 positive cases. Overall, the Idylla assay generated valid results in 96.4% (53/55) of the samples. A 96.2% (51/53) concordance rate between the Idylla SARS-CoV-2 Test and the Real-Time SARS-CoV-2 kit has been obtained. No false positive results have been reported (specificity 100.0%). These results demonstrated that the Idylla SARS-CoV-2 Test may represent a valid, fast, highly sensitive and specific RT-PCR test for the identification of SARS-CoV-2 infection.
Care and Treatment

- This randomised, controlled, open-label, platform trial in the United Kingdom evaluated the use of baricitinib, a Janus kinase (JAK) 1–2 inhibitor, for the treatment of patients admitted to hospital with COVID-19. The study involved 8,156 patients who were randomly allocated (1:1) to receive usual care plus baricitinib (4 mg once daily by mouth for 10 days or until discharge if sooner) versus usual care alone. Overall, 514/4148 (12%) patients allocated to baricitinib versus 546/4008 (14%) patients allocated to usual care died within 28 days (age-adjusted rate ratio 0.87; 95% CI 0.77–0.99; p=0.028). Including the results from RECOVERY in an updated meta-analysis of all nine completed trials (involving 11,888 randomly assigned patients and 1,485 deaths) allocation to baricitinib or another JAK inhibitor was associated with a 20% proportional reduction in mortality (rate ratio 0.80; 95% CI 0.72–0.89; p<0.0001).

- This prospective cohort study conducted in 8 countries assessed the proportion of and factors associated with post-COVID-19 conditions (PCCs) 90 days after a positive test result among children. The study involved 8642 children across 36 emergency departments between March 2020 and January 2021. A total of 1884 SARS-CoV-2–positive children with 90-day follow-up, 5.8% of patients, including 9.8% of hospitalised children and 4.6% of discharged children, reported PCCs. Characteristics associated with PCCs included being hospitalised 48 hours or more compared with no hospitalisation (aOR, 2.67 [95% CI, 1.63–4.38]), having 4 or more symptoms reported at the index ED visit compared with 1 to 3 symptoms (4–6 symptoms: aOR, 2.35 [95% CI, 1.28–4.31]; ≥7 symptoms: aOR, 4.59 [95% CI, 2.50–8.44]); and being 14 years of age or older compared with younger than 1 year (aOR, 2.67 [95% CI, 1.43–4.99]). This study suggests that, given the prevalence of PCCs, appropriate guidance and follow-up are required for children testing positive for SARS-CoV-2.

- This modelling study in the United States and China proposes an accurate, time-efficient, and versatile approach for segmentation and scoring of lung diseases including COVID-19. The models of the proposed workflow were trained and tested on four publicly available X-ray datasets of COVID-19 patients and two X-ray datasets of patients with no pulmonary pathology. The study involved a combined dataset consisting of 580 COVID-19 patients and 784 patients with no disorders, the algorithm is based on a combination of DeepLabV3+, for lung segmentation, and MA-Net, for disease segmentation. The proposed algorithms’ mean absolute error (MAE) of 0.30 is significantly reduced in comparison to established COVID-19 algorithms; BS-net and COVID-Net-S, possessing MAEs of 2.52 and 1.83 respectively. The proposed two-stage workflow was approximately 11 times faster than the mentioned methods.

- This prospective cohort study in Canada assessed the 1-year outcomes among non-hospitalised survivors of COVID-19 using both a telephone and online questionnaire-based assessment. Among 81 adults who completed online assessments at 3 and 12-months following infection, quality of life scores did not significantly improve over time. Among 62 subjects who also completed telephone interviews, respiratory symptoms or exercise limitation were reported by 42% at a median follow-up of 387 days (IQR 251–402 days). Those with persistent respiratory symptoms scored lower on the EQ-5D visual analog score compared to those without. Persistent respiratory symptoms were associated with a lower likelihood of full-time employment at 1-year (aOR 0.09, 95%CI 0.01–0.91; p = 0.041). In an adjusted linear regression, persistent respiratory symptoms (p = 0.037) and female sex (p = 0.016) were both independent risks for increased visits to a primary care provider. This cohort study demonstrates that respiratory symptoms are frequent at 1-year following COVID-19 and more importantly, are associated with negative impacts on employment, quality of life, and health care utilization.

- This case series in Scotland characterised hemidiaphragm elevation on 3-month interval chest X-rays (CXRs) of patients post COVID-19 pneumonia. The study involved 467 patients with COVID-19 pneumonia from March 2020 to January 2021. There were 15 (3.2%) patients of interest with new hemidiaphragm elevation, persisting on average 7 months post COVID-19 diagnosis. Symptomatic patients underwent diaphragm ultrasound (n=12), pulmonary function test (n=10), muscle function test (n=6) and neurophysiology (n=5), investigating phrenic nerve function. Ultrasound demonstrated reduced/paradoxical diaphragmatic movements in eight; four of eight had reduced thickening fraction. Neurophysiology peripheral limb studies did not support the differential diagnoses of critical illness.
neuropathy/myopathy. The authors propose that, in selected patients, COVID-19 may cause phrenic nerve mononeuritis. They recommend future prospective studies to assess whether diaphragmatic dysfunction aids prognostication in COVID-19.

Epidemiology

- This study documents the presence of antibodies against SARS-CoV-2 N and S proteins in pre-pandemic sera (collected prior to November 2019) from individuals from various continents as well as the in vitro neutralisation capacity and the in vivo protective efficacy of some of the sera with high antibody levels against SARS-CoV-2 N protein. The study involved testing serum from 43, 121, 112 and 146 individuals from Quebec (Canada), Denmark, Brazil and Gabon. Antibodies against SARS-CoV-2 S and N proteins were rare in all populations except in Gabon and Senegal where N specific antibodies were prevalent. However, these antibodies failed to neutralise the virus either in vitro or in vivo. Overall, this study indicates that cross-reactive immunity against SARS-CoV-2 N protein was present in Africa prior to the pandemic. However, this pre-existing humoral immunity does not impact viral fitness in rodents suggesting that other human immune defence mechanisms could be involved.

- This retrospective cohort study in the United Kingdom and Switzerland combined dynamic networks of patient contacts (based on bed allocation records) with clinical attributes and hospital contextual data into a novel forecasting framework to predict patient risk of hospital-onset COVID-19 infections (HOCIs) acquisition for targeting preventive interventions. The study utilised data from 51157 hospital inpatients in the UK and 40,057 inpatients in Switzerland. The framework was highly predictive across test data with all variable types (area under the curve [AUC]-receiver operating characteristic curve [ROC] 0.89 [95% CI 0.88–0.90]) and similarly predictive using only contact-network variables (0.88 [0.86–0.90]). Prediction was reduced when using only hospital contextual (AUC-ROC 0.82 [95% CI 0.80–0.84]) or patient clinical (0.64 [0.62–0.66]) variables. A model with only three variables (ie, network closeness, direct contacts with infectious patients [network derived], and hospital COVID-19 prevalence [hospital contextual]) achieved AUC-ROC 0.85 (95% CI 0.82–0.88). Their framework can be used in real time to generate daily risk predictions as part of a suite of surveillance tools in modern, data-driven infection prevention and control strategies.

- This modelling study in the United Kingdom assessed the best prevention strategy to maximize on-campus activities while keeping COVID-19 spread under control. The model takes into account staff-to-staff infections, student-to-staff cross infections, student-to-student infections, and environment-to-individual infections. Their results reveal the particular significance of mask wearing and social distancing in universities with a vaccinated population. In a typical university department composed of 1200 students and 150 staff, with a vaccination rate of 68% for students and 78.8% for staff, implementation of non-pharmaceutical interventions is still fundamental to reduce the number of infections to one tenth of the number of infections appearing in a completely uncontrolled scenario. The study also reveals that quarantining infected students has a higher importance than quarantining staff.

- This study in the United States obtained data from a range of sources and tested the hypothesis that the COVID-19 pandemic began at the Huanan market. Live SARS-CoV-2 susceptible mammals were sold at the market in late 2019 and, within the market, SARS-CoV-2-positive environmental samples were spatially associated with vendors selling live mammals. Despite limited testing of live wildlife sold at the market, collectively, their results provide evidence that the Huanan market was the early epicentre of the COVID-19 pandemic and suggest that SARS-CoV-2 likely emerged from the live wildlife trade in China. However, events upstream of the market, as well as exact circumstances at the market, remain obscure, highlighting the need for further studies to understand and lower the risk of future pandemics.

Infection Prevention & Control

- This study in Japan assessed the neutralising ability of FDA-approved monoclonal antibodies, individually and in combination, against omicron BA.2.12.1, BA.4 and BA.5 isolates. Live-virus focus reduction neutralisation testing (FRNT) showed that casirivimab lost neutralising activity against
BA.2.12.1, BA.4, and BA.5. However, imdevimab retained neutralising activity against these isolates. The combination of casirivimab and imdevimab also inhibited BA.2.12.1, BA.4, and BA.5; however, the value of this combination was higher on 50% focus reduction neutralisation testing (FRNT\textsubscript{50}) by a factor of 131.6 against BA.2.12.1, by a factor of 133.5 against BA.4, and by a factor of 317.8 against BA.5 than against the ancestral strain. Tixagevimab had neutralising activity against BA.2.12.1 but not against BA.4 or BA.5. However, cilgavimab neutralised BA.2.12.1, BA.4, and BA.5. The combination of tixagevimab and cilgavimab inhibited BA.2.12.1, BA.4, and BA.5, with a low FRNT\textsubscript{50} value (38.1 ng/ml, 37.8 ng/ml, and 192.5 ng/ml, respectively). However, as compared with the FRNT\textsubscript{50} value against the ancestral strain, the FRNT\textsubscript{50} value of this combination was higher by a factor of 6.1 against BA.2.12.1, by a factor of 6.0 against BA.4, and by a factor of 30.7 against BA.5. The precursor of sotrovimab lost inhibitory capability against BA.2.12.1, BA.4, and BA.5. Of the FDA-approved monoclonal antibodies that were tested, only bebtelovimab efficiently neutralised BA.2.12.1, BA.4, and BA.5; the FRNT\textsubscript{50} values for these isolates were similar to those for the ancestral strain. These findings show that the selection of monoclonal antibodies to treat patients who are infected with omicron variants should be carefully considered.

- This phase 3, randomised, double-blind, placebo-controlled trial in the United States assessed immune responses to full COVID-19 vaccination with either mRNA-1273 or BNT162b2 mRNA vaccines after passive immunization with bamlanivimab administered as a COVID-19 prevention intervention for participants who were residents or staff of skilled nursing and assisted living facilities. The study involved 135 participants. Antibody titres and potency were assessed using three assays against SARS-CoV-2 proteins that bamlanivimab does not efficiently bind to, thereby reflecting the endogenous antibody response. All bamlanivimab and placebo recipients mounted a robust immune response to full COVID-19 vaccination, irrespective of age, risk category, and vaccine type with any observed differences of uncertain clinical importance. These findings are pertinent for informing public health policy with results that suggest that the benefit of receiving COVID-19 vaccination at the earliest opportunity outweighs the minimal effect on the endogenous immune response due to prior prophylactic COVID-19 monoclonal antibody infusion.

**Non-pharmaceutical interventions, social distancing**

- This non-randomised controlled study in Spain assessed whether people who attended public events with a certified low risk of transmitting SARS-CoV-2 infection presented a higher rate of detected SARS-CoV-2 infections compared to a group of people who did not attend such events. The digital pass certified a negative antigen test result, or immunity against SARS-CoV-2 (confirmed vaccination or recovery from COVID-19). The study involved 1351 participants who were matched with 4050 controls between 1 April and 21 May 2021. Incidence rates of SARS-CoV-2 infection at 14 days in the group of attendees and non-attendees were 15.9 and 17.7 per 100,000 person-days, respectively; the difference between incidences was −1.8 (95% CI –22.8, 19.3). Implementation problems were minor, and 89.2% of respondents to a survey were satisfied with the process. The incidence rate of SARS-CoV-2 infection was not different in the intervention and control groups. These results are in favour of establishing a COVID-19 certificate to attend public events, and connote feasibility of implementation at a population level.

**D. Clinical Trials Updates**

**Key updates:**

**Vaccine trials:**

- On 29 July 2022, Novavax announced the submission of a request to the World Health Organization (WHO) to expand the Emergency Use Listing (EUL) of Nuvaxovid (NVX-CoV2373) COVID-19 vaccine for active immunization to prevent COVID-19 in adolescents aged 12 through 17. The request 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 United States. The Trial is evaluating 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. No new safety signal was observed through the placebo-controlled portion of the study. Clinical trial registration #: (NCT04611802).

On 29 July 2022, GreenLight Biosciences announced a collaboration with the National Institutes of Health (NIH) to develop COVID-19 vaccines that are more broadly protective against new variants and with longer-lasting effects. They will co-design and test mRNA vaccines against coronaviruses with the goal of developing vaccines that confer a more durable immune response than current vaccines. SARS-CoV-2, the virus that causes COVID-19, continues to evolve and accumulate genomic mutations with the potential to negatively affect the efficacy of existing medical countermeasures. For the current COVID-19 pandemic and future coronavirus-related pandemics, the rapid development and deployment of vaccines active against a range of coronaviruses, including variants of SARS-CoV-2, will be vital for public health.

On 27 July 2022, Pfizer and BioNTech announced they have initiated a randomised, active-controlled, observer-blind, Phase 2 study to evaluate the safety, tolerability, and immune response of an enhanced COVID-19 mRNA-based vaccine candidate at a 30 µg dose level. This next-generation bivalent COVID-19 vaccine candidate, BNT162b5, consists of RNAs encoding enhanced prefusion spike proteins for the SARS-CoV-2 ancestral strain (wild-type) and an Omicron variant. BNT162b5 will be evaluated in a U.S.-based study enrolling approximately 200 participants aged between 18 and 55 who have received one booster dose of a U.S.-authorized COVID-19 vaccine at least 90 days prior to their first study visit. Participants will be stratified by the number of months since their last dose of COVID-19 vaccine received prior to entering the study (three to six months or more than six months). The enhanced spike protein encoded from the mRNAs in BNT162b5 has been modified with the aim of increasing the magnitude and breadth of the immune response that could better protect against COVID-19. Clinical trial registration #: (NCT05472038).

On 26 July 2022, Novavax announced the Australian Therapeutic Goods Agency (TGA) has granted expanded approval for provisional registration of Nuvaxovid (NVX-CoV2373) COVID-19 vaccine for active immunization to prevent COVID-19 in adolescents aged 12 through 17 years. The provisional registration based on data from the ongoing paediatric expansion of PREVENT-19, a pivotal Phase 3 trial of 2,247 adolescents aged 12 through 17 years across 73 sites in the U.S., to evaluate the safety, effectiveness (immunogenicity), and efficacy of Nuvaxovid. In the trial, Nuvaxovid achieved its primary effectiveness endpoint and demonstrated 80% clinical efficacy overall at a time when the Delta variant was the predominant circulating SARS-CoV-2 strain in the U.S. Clinical trial registration #: (NCT04611802).

On 22 July 2022, Moderna announced that 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 booster dose of Spikevax, COVID-19 vaccine at the 50 µg dose level for adolescents (12-17 years) at least three months after completion of the primary series. The CHMP based this positive opinion on available scientific evidence including comprehensive safety data. The administration of a booster dose of 50 µg at least three months after administration of completion of the primary series is predicted to substantially increase the immune responses against variants of concern, including Omicron compared to pre-boost levels.
On 19 July 2022, Novavax announced that the U.S. Centers for Disease Control and Prevention’s (CDC) Advisory Committee on Immunization Practices (ACIP) voted unanimously to recommend the use of the Novavax COVID-19 Vaccine, Adjuvanted as a two-dose primary series in individuals aged 18 and older. The recommendation based on data from the pivotal Phase 3 clinical trial, PREVENT-19, which enrolled 29,960 participants aged 18 years and older in the U.S. and Mexico. In the trial, the Novavax COVID-19 Vaccine, Adjuvanted demonstrated 90.4% efficacy (95% confidence interval [CI], 83.8% to 94.3%; P<0.001) with a reassuring safety profile. Clinical trial registration #: (NCT04611802).

Therapeutics trials:

- On 2 August 2022, Axcella Therapeutics reported top-line results from the Phase 2a randomised, double-blind, placebo-controlled investigation to evaluate the efficacy and safety of AXA1125 in patients with fatigue related to Long COVID. AXA1125 is a mixture of amino acids that can combat fatigue by restoring mitochondria function. In the study, 41 subjects were enrolled and randomised to receive either 67.8 grams per day of AXA1125 (N=21) or a matched placebo (N=20) in two divided doses for 28 days, with a one-week safety follow-up period. Subjects who received AXA1125 had improvements in measures of mental and physical fatigue that were both highly statistically significant and clinically relevant compared to those who received placebo. Mean changes in total, physical and mental scores in the Chalder Fatigue Questionnaire (CFQ)-11 versus placebo were -4.30 (p=0.0039), -2.94 (p=0.0097) and -1.32 (p=0.0097), respectively. Clinically meaningful shifts in the severity of physical and mental fatigue were also noted in subjects who received AXA1125 compared to those who received placebo. There was a statistically significant correlation of improvement in fatigue score and greater distance achieved in the 6-minute walk test (6MWT) (p=0.0027), an objective measure of physical ability, only observed in subjects who received AXA1125 compared to those who received placebo. There was no significant difference on the primary outcome measure of phosphocreatine recovery time (PCrτ) following moderate exercise between subjects receiving AXA1125 and placebo. There was a notable trend toward significant improvement in serum lactate levels after a 6MWT in AXA1125 subjects (p=0.0730). AXA1125 was safe and well tolerated with no significant adverse events reported by study subjects. Clinical trial registration #: (NCT05152849).

- On 27 July 2022, AIM ImmunoTech reported positive preliminary pilot study data from its ongoing Expanded Access Program (“EAP or “AMP-511”) evaluating its investigational drug, Ampligen, as a therapeutic for “long COVID”. Ampligen is RNA product candidate being developed for globally important cancers, viral diseases and disorders of the immune system. Ampligen modulates the immune system and has demonstrated antiviral activity. The preliminary data from this uncontrolled clinical trial found that patients reported statistically significant improvements in chronic fatigue after treatment with Ampligen. Based on these early results, AIM is working to move forward with a Phase 2 controlled trial. AMP-511 is an ongoing, prospective, open-label, multi-center Phase 3 study to treat myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) patients with Ampligen. Clinical trial registration #: (NCT04765449).

- On 27 July 2022, Veru announced that the European Medicines Agency’s (EMA) Emergency Task Force (ETF) has initiated the review of sabizabulin for the treatment of hospitalised COVID-19 patients at high risk for Acute Respiratory Distress Syndrome (ARDS). Sabizabulin is an orally bioavailable bis-indole that binds to the “colchicine binding site” of alpha and beta tubulin and inhibits tubulin polymerization at low nanomolar concentrations. Sabizabulin disrupts the microtubules, the central mechanism that contributes to both their antiviral and anti-inflammatory activities. Sabizabulin that target microtubules have broad antiviral activity by disrupting the intracellular transport of viruses including SARS CoV-2 that causes COVID 19. The ETF will review all available data, including data
Immunotheapies trials:

- On 1 August 2022, Tevogen announced that it completed enrolment in the Proof-of-Concept clinical trial of the lead investigational product, TVGN-489, for elderly or high-risk ambulatory COVID-19 patients. TVGN-489 is a genetically unmodified, off-the-shelf, allogeneic cytotoxic CD8+ T lymphocyte (CTL) product with activity against multiple, precise targets across the SARS-CoV-2 genome. The open-label clinical trial was designed to study the safety and optimal dose of TVGN-489 when given to ambulatory patients with newly diagnosed COVID-19 infection who were at higher risk for infection-related complications. Clinical trial registration #: (NCT04765449).

- On 26 July 2022, Brii Biosciences announced new live virus data confirming that the amubarvimab/romlusevimab combination, a long-acting COVID-19 monoclonal antibody (mAb) therapy, retains neutralising activity against the Omicron BA.4/5 and BA.2.12.1 SARS-CoV-2 subvariants. Data from the live virus neutralisation assay performed at a University of Maryland lab certified by the U.S. National Institutes of Health (NIH) and National Institute of Allergy and Infectious Diseases (NIAID) predict that total serum concentrations of the amubarvimab/romlusevimab combination will remain greater than 170 times the level required for greater than 90% neutralisation (Neut99: 0.94 μg/mL) against the live virus, 14 days post dose. As a result, adequate therapeutic exposures are expected to persist throughout the treatment period. Amubarvimab and Romlusevimab are non-competing SARS-CoV-2 monoclonal neutralising antibodies derived from convalesced COVID-19 patients developed in collaboration with the 3rd People’s Hospital of Shenzhen and Tsinghua University. They have been specifically engineered to reduce the risk of antibody-dependent enhancement and prolong the plasma half-lives for potentially more durable treatment effect. Based on the final results from ACTIV-2 Phase 3 clinical trial with 837 enrolled outpatients, the amubarvimab/romlusevimab combination demonstrates a statistically significant 80% reduction of hospitalisation and death with fewer deaths through 28 days in the treatment arm (0) relative to placebo (9), and improved safety outcome over placebo in non-hospitalised COVID-19 patients at high risk of clinical progression to severe disease. Similar efficacy rates were observed in participants initiating therapy early (0-5 days) and late (6-10 days), following symptom onset, providing critically needed clinical evidence in COVID-19 patients who were late for treatment. Clinical trial registration #: (NCT04518410).

Contributors
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