COVID-19 weekly update

February 14th 2022

**clinical management**

**Title:** Risk of persistent and new clinical sequelae among adults aged 65 years and older during the post-acute phase of SARS-CoV-2 infection: retrospective cohort study

bmj| 9th February

**Objective** To characterize the risk of persistent and new clinical sequelae in adults aged ≥65 years after the acute phase of SARS-CoV-2 infection.

**Design** Retrospective cohort study.

**Setting** UnitedHealth Group Clinical Research Database: deidentified administrative claims and outpatient laboratory test results.

**Participants** Individuals aged ≥65 years who were continuously enrolled in a Medicare Advantage plan with coverage of prescription drugs from January 2019 to the date of diagnosis of SARS-CoV-2 infection, matched by propensity score to three comparison groups that did not have covid-19: 2020 comparison group (n=87 337), historical 2019 comparison group (n=88 070), and historical comparison group with viral lower respiratory tract illness (n=73 490).

**Main outcome measures** The presence of persistent and new sequelae at 21 or more days after a diagnosis of covid-19 was determined with ICD-10 (international classification of diseases, 10th revision) codes. Excess risk for sequelae caused by infection with SARS-CoV-2 was estimated for the 120 days after the acute phase of the illness with risk difference and hazard ratios, calculated with 95% Bonferroni corrected confidence intervals. The incidence of sequelae after the acute infection was analyzed by age, race, sex, and whether patients were admitted to hospital for covid-19.

**Results** Among individuals who were diagnosed with SARS-CoV-2, 32% (27 698 of 87 337) sought medical attention in the post-acute period for one or more new or persistent clinical sequelae, which was 11% higher than the 2020 comparison group. Respiratory failure (risk difference 7.55, 95% confidence interval 7.18 to 8.01), fatigue (5.66, 5.03 to 6.27), hypertension (4.43, 2.27 to 6.37), memory difficulties (2.63, 2.23 to 3.13), kidney injury (2.59, 2.03 to 3.12), mental health diagnoses (2.50, 2.04 to 3.04), hypercoagulability 1.47 (1.2 to 1.73), and cardiac rhythm disorders (2.19, 1.76 to 2.57) had the greatest risk differences compared with the 2020 comparison group, with similar findings to the 2019 comparison group. Compared with the group with viral lower respiratory tract illness, however, only respiratory failure, dementia, and post-viral fatigue had increased risk differences of 2.39 (95% confidence interval 1.79 to 2.94), 0.71 (0.3 to 1.08), and 0.18 (0.11 to 0.26) per 100 patients, respectively. Individuals with severe covid-19 disease requiring admission to hospital had a markedly increased risk for most but not all clinical sequelae.

**Conclusions** The results confirm an excess risk for persistent and new sequelae in adults aged ≥65 years after acute infection with SARS-CoV-2. Other than respiratory failure, dementia, and post-viral fatigue, the sequelae resembled those of viral lower respiratory tract illness in older adults. These findings further highlight the wide range of important sequelae after acute infection with the SARS-CoV-2 virus.

Full article: [Risk of persistent and new clinical sequelae among adults aged 65 years and older during the post-acute phase of SARS-CoV-2 infection: retrospective cohort study | The BMJ](https://www.bmj.com/content/376/bmj-2021-068414)

**Title:** Casirivimab and imdevimab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial

the lancet| 12th February

Background

Casirivimab and imdevimab are non-competing monoclonal antibodies that bind to two different sites on the receptor binding domain of the SARS-CoV-2 spike glycoprotein, blocking viral entry into host cells. We aimed to evaluate the efficacy and safety of casirivimab and imdevimab administered in combination in patients admitted to hospital with COVID-19.

Methods

RECOVERY is a randomised, controlled, open-label platform trial comparing several possible treatments with usual care in patients admitted to hospital with COVID-19. 127 UK hospitals took part in the evaluation of casirivimab and imdevimab. Eligible participants were any patients aged at least 12 years admitted to hospital with clinically suspected or laboratory-confirmed SARS-CoV-2 infection. Participants were randomly assigned (1:1) to either usual standard of care alone or usual care plus casirivimab 4 g and imdevimab 4 g administered together in a single intravenous infusion. Investigators and data assessors were masked to analyses of the outcome data during the trial. The primary outcome was 28-day all-cause mortality assessed by intention to treat, first only in patients without detectable antibodies to SARS-CoV-2 infection at randomisation (ie, those who were seronegative) and then in the overall population. Safety was assessed in all participants who received casirivimab and imdevimab. The trial is registered with ISRCTN (50189673) and [ClinicalTrials.gov](http://clinicaltrials.gov/) ([NCT04381936](http://clinicaltrials.gov/show/NCT04381936)).

Findings

Between Sept 18, 2020, and May 22, 2021, 9785 patients enrolled in RECOVERY were eligible for casirivimab and imdevimab, of which 4839 were randomly assigned to casirivimab and imdevimab plus usual care and 4946 to usual care alone. 3153 (32%) of 9785 patients were seronegative, 5272 (54%) were seropositive, and 1360 (14%) had unknown baseline antibody status. 812 (8%) patients were known to have received at least one dose of a SARS-CoV-2 vaccine. In the primary efficacy population of seronegative patients, 396 (24%) of 1633 patients allocated to casirivimab and imdevimab versus 452 (30%) of 1520 patients allocated to usual care died within 28 days (rate ratio [RR] 0·79, 95% CI 0·69–0·91; p=0·0009). In an analysis of all randomly assigned patients (regardless of baseline antibody status), 943 (19%) of 4839 patients allocated to casirivimab and imdevimab versus 1029 (21%) of 4946 patients allocated to usual care died within 28 days (RR 0·94, 95% CI 0·86–1·02; p=0·14). The proportional effect of casirivimab and imdevimab on mortality differed significantly between seropositive and seronegative patients (p value for heterogeneity=0·002). There were no deaths attributed to the treatment, or meaningful between-group differences in the pre-specified safety outcomes of cause-specific mortality, cardiac arrhythmia, thrombosis, or major bleeding events. Serious adverse reactions reported in seven (<1%) participants were believed by the local investigator to be related to treatment with casirivimab and imdevimab.

Interpretation

In patients admitted to hospital with COVID-19, the monoclonal antibody combination of casirivimab and imdevimab reduced 28-day mortality in patients who were seronegative (and therefore had not mounted their own humoral immune response) at baseline but not in those who were seropositive at baseline.

Full article: [Casirivimab and imdevimab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial - The Lancet](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2900163-5/fulltext)

**Title:** High-titre methylene blue-treated convalescent plasma as an early treatment for outpatients with COVID-19: a randomised, placebo-controlled trial

the lancet respiratory medicine| 9th February

Background

Convalescent plasma has been proposed as an early treatment to interrupt the progression of early COVID-19 to severe disease, but there is little definitive evidence. We aimed to assess whether early treatment with convalescent plasma reduces the risk of hospitalisation and reduces SARS-CoV-2 viral load among outpatients with COVID-19.

Methods

We did a multicentre, double-blind, randomised, placebo-controlled trial in four health-care centres in Catalonia, Spain. Adult outpatients aged 50 years or older with the onset of mild COVID-19 symptoms 7 days or less before randomisation were eligible for enrolment. Participants were randomly assigned (1:1) to receive one intravenous infusion of either 250–300 mL of ABO-compatible high anti-SARS-CoV-2 IgG titres (EUROIMMUN ratio ≥6) methylene blue-treated convalescent plasma (experimental group) or 250 mL of sterile 0·9% saline solution (control). Randomisation was done with the use of a central web-based system with concealment of the trial group assignment and no stratification. To preserve masking, we used opaque tubular bags that covered the investigational product and the infusion catheter. The coprimary endpoints were the incidence of hospitalisation within 28 days from baseline and the mean change in viral load (in log10 copies per mL) in nasopharyngeal swabs from baseline to day 7. The trial was stopped early following a data safety monitoring board recommendation because more than 85% of the target population had received a COVID-19 vaccine. Primary efficacy analyses were done in the intention-to-treat population, safety was assessed in all patients who received the investigational product. This study is registered with [ClinicalTrials.gov](http://clinicaltrials.gov/), [NCT04621123](http://clinicaltrials.gov/show/NCT04621123).

Findings

Between Nov 10, 2020, and July 28, 2021, we assessed 909 patients with confirmed COVID-19 for inclusion in the trial, 376 of whom were eligible and were randomly assigned to treatment (convalescent plasma n=188 [serum antibody-negative n=160]; placebo n=188 [serum antibody-negative n=166]). Median age was 56 years (IQR 52–62) and the mean symptom duration was 4·4 days (SD 1·4) before random assignment. In the intention-to-treat population, hospitalisation within 28 days from baseline occurred in 22 (12%) participants who received convalescent plasma versus 21 (11%) who received placebo (relative risk 1·05 [95% CI 0·78 to 1·41]). The mean change in viral load from baseline to day 7 was −2·41 log10 copies per mL (SD 1·32) with convalescent plasma and −2·32 log10 copies per mL (1·43) with placebo (crude difference −0·10 log10 copies per mL [95% CI −0·35 to 0·15]). One participant with mild COVID-19 developed a thromboembolic event 7 days after convalescent plasma infusion, which was reported as a serious adverse event possibly related to COVID-19 or to the experimental intervention.

Interpretation

Methylene blue-treated convalescent plasma did not prevent progression from mild to severe illness and did not reduce viral load in outpatients with COVID-19. Therefore, formal recommendations to support the use of convalescent plasma in outpatients with COVID-19 cannot be concluded.

Full article: [High-titre methylene blue-treated convalescent plasma as an early treatment for outpatients with COVID-19: a randomised, placebo-controlled trial - The Lancet Respiratory Medicine](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600%2821%2900545-2/fulltext)

**Title:** Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients

NEJM| 10th february

**BACKGROUND**

New treatments are needed to reduce the risk of progression of coronavirus disease 2019 (Covid-19). Molnupiravir is an oral, small-molecule antiviral prodrug that is active against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

**METHODS**

We conducted a phase 3, double-blind, randomized, placebo-controlled trial to evaluate the efficacy and safety of treatment with molnupiravir started within 5 days after the onset of signs or symptoms in nonhospitalized, unvaccinated adults with mild-to-moderate, laboratory-confirmed Covid-19 and at least one risk factor for severe Covid-19 illness. Participants in the trial were randomly assigned to receive 800 mg of molnupiravir or placebo twice daily for 5 days. The primary efficacy end point was the incidence hospitalization or death at day 29; the incidence of adverse events was the primary safety end point. A planned interim analysis was performed when 50% of 1550 participants (target enrollment) had been followed through day 29.

**RESULTS**

A total of 1433 participants underwent randomization; 716 were assigned to receive molnupiravir and 717 to receive placebo. With the exception of an imbalance in sex, baseline characteristics were similar in the two groups. The superiority of molnupiravir was demonstrated at the interim analysis; the risk of hospitalization for any cause or death through day 29 was lower with molnupiravir (28 of 385 participants [7.3%]) than with placebo (53 of 377 [14.1%]) (difference, −6.8 percentage points; 95% confidence interval [CI], −11.3 to −2.4; P=0.001). In the analysis of all participants who had undergone randomization, the percentage of participants who were hospitalized or died through day 29 was lower in the molnupiravir group than in the placebo group (6.8% [48 of 709] vs. 9.7% [68 of 699]; difference, −3.0 percentage points; 95% CI, −5.9 to −0.1). Results of subgroup analyses were largely consistent with these overall results; in some subgroups, such as patients with evidence of previous SARS-CoV-2 infection, those with low baseline viral load, and those with diabetes, the point estimate for the difference favored placebo. One death was reported in the molnupiravir group and 9 were reported in the placebo group through day 29. Adverse events were reported in 216 of 710 participants (30.4%) in the molnupiravir group and 231 of 701 (33.0%) in the placebo group.

**CONCLUSIONS**

Early treatment with molnupiravir reduced the risk of hospitalization or death in at-risk, unvaccinated adults with Covid-19. (Funded by Merck Sharp and Dohme; MOVe-OUT ClinicalTrials.gov number, [**NCT04575597. opens in new tab**](http://clinicaltrials.gov/show/NCT04575597).)

Full article: [Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients | NEJM](https://www.nejm.org/doi/full/10.1056/NEJMoa2116044)

**Title:** Efficacy of Niclosamide vs Placebo in SARS-CoV-2 Respiratory Viral Clearance, Viral Shedding, and Duration of Symptoms Among Patients With Mild to Moderate COVID-19

jama network open| 9th february

**Question**  Does oral niclosamide decrease the contagious period as determined by SARS-CoV-2 shedding among patients with mild to moderate COVID-19?

**Findings**  In this randomized clinical trial that included 73 adults with mild to moderate COVID-19, the proportion of participants achieving oropharyngeal clearance of SARS-CoV-2 at 3 days postenrollment was not statistically significantly different between patients given placebo and those given niclosamide. Niclosamide was well-tolerated.

**Meaning**  This study did not find a significant effect of niclosamide on decreasing the contagious period of SAR-CoV-2 infection.

Full article: [Efficacy of Niclosamide vs Placebo in SARS-CoV-2 Respiratory Viral Clearance, Viral Shedding, and Duration of Symptoms Among Patients With Mild to Moderate COVID-19: A Phase 2 Randomized Clinical Trial | Infectious Diseases | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788857)

**Title:** Characteristics, Outcomes, and Severity Risk Factors Associated With SARS-CoV-2 Infection Among Children in the US National COVID Cohort Collaborative

jama network open| 8th february

**Question**  What are the characteristics, changes over time, outcomes, and severity risk factors of children with SARS-CoV-2 within the National COVID Cohort Collaborative?

**Findings**  In this cohort study, 167 262 children at 56 sites were SARS-CoV-2–positive and 10 245 were hospitalized. Several demographic and comorbidity variables and many initial vital sign and laboratory test values were associated with higher peak illness severity.

**Meaning**  This study noted clinical data elements that could assist with early identification of children at risk for severe disease due to SARS-CoV-2 infection.

Full article: [Characteristics, Outcomes, and Severity Risk Factors Associated With SARS-CoV-2 Infection Among Children in the US National COVID Cohort Collaborative | Pediatrics | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788844)

**recovery**

**Title:** Covid-19: Pandemic has harmed cancer outcomes and widened inequalities, report finds

Bmj| 11th February

The covid-19 pandemic has impaired referrals for preliminary cancer diagnoses and led to an 11% increase in patients diagnosed with inoperable or metastatic cancer in the US in 2020, a new report has found.

The report by the American Association for Cancer Research (AACR) on the impact of covid-19 on cancer research and patient care,[**1**](https://www.bmj.com/content/376/bmj.o375#ref-1) released on 9 February, also noted that nearly 10 million patients missed cancer screenings during the first six months of the year, resulting in later diagnoses and poorer outcomes.

In a briefing to discuss the report organised by AACR, Philadelphia oncologist Ana Marie Lopez drew attention to the finding that the pandemic had struck medically underserved communities hardest, particularly people of colour.

Full news article: [Covid-19: Pandemic has harmed cancer outcomes and widened inequalities, report finds | The BMJ](https://www.bmj.com/content/376/bmj.o375)

**Title:** Health leaders question absence of workforce strategy in NHS elective care recovery plan

bmj| 8th February

The government has promised to build more surgical and community diagnostic hubs in England and to give patients greater control over their healthcare provider as part of its long awaited recovery plan for elective care to reduce the NHS backlog and tackle waiting times.1

But the targets set out on 8 February will not be met without the staff to run the expanded services, health leaders have warned.

Andrew Goddard, president of the Royal College of Physicians, said that the plan depended on the “recovery of urgent and emergency care, as the two are intimately entwined both with respect to workforce and estate.”

Full news article: [Health leaders question absence of workforce strategy in NHS elective care recovery plan | The BMJ](https://www.bmj.com/content/376/bmj.o343)

[Health Management and Policy Alert: Delivery plan for tackling the Covid-19 backlog of elective care (blogs.com)](https://kingsfund.blogs.com/health_management/2022/02/delivery-plan-for-tackling-the-covid-19-backlog-of-elective-care.html)

[Health Management and Policy Alert: NHSE/I delivery plan for tackling the backlog of elective care (blogs.com)](https://kingsfund.blogs.com/health_management/2022/02/nhsei-delivery-plan-for-tackling-the-backlog-of-elective-care-.html)

**Title:** State Of The Nation 2021: Children And Young People’s Wellbeing

Department for Education| 8th February

This report collates and presents new analysis of published evidence on the wellbeing of children and young people over the period of August 2020 to July 2021, including statistics on the personal wellbeing of children and young people in England and the UK and a wider set of indicators on their: mental and physical health; education and skills; relationships; activities and time use; views on the self, society, and future; an analysis of Covid-19 and the psychological health of young adults; and an analysis of individual predictors of school attendance in 2020 to 2021.

* [Report](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1053302/State_of_the_Nation_CYP_Wellbeing_2022.pdf)
* [Press release](https://www.gov.uk/government/news/improvements-seen-in-children-and-young-peoples-wellbeing)

**Infection control**

**Title:** Effectiveness of mRNA vaccines and waning of protection against SARS-CoV-2 infection and severe covid-19 during predominant circulation of the delta variant in Italy: retrospective cohort study

BMJ| 10th february

**Objectives** To estimate the effectiveness of mRNA vaccines against SARS-CoV-2 infection and severe covid-19 at different time after vaccination.

**Design** Retrospective cohort study.

**Setting** Italy, 27 December 2020 to 7 November 2021.

**Participants** 33 250 344 people aged ≥16 years who received a first dose of BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) vaccine and did not have a previous diagnosis of SARS-CoV-2 infection.

**Main outcome measures** SARS-CoV-2 infection and severe covid-19 (admission to hospital or death). Data were divided by weekly time intervals after vaccination. Incidence rate ratios at different time intervals were estimated by multilevel negative binomial models with robust variance estimator. Sex, age group, brand of vaccine, priority risk category, and regional weekly incidence in the general population were included as covariates. Geographic region was included as a random effect. Adjusted vaccine effectiveness was calculated as (1−IRR)×100, where IRR=incidence rate ratio, with the time interval 0-14 days after the first dose of vaccine as the reference.

**Results** During the epidemic phase when the delta variant was the predominant strain of the SARS-CoV-2 virus, vaccine effectiveness against SARS-CoV-2 infection significantly decreased (P<0.001) from 82% (95% confidence interval 80% to 84%) at 3-4 weeks after the second dose of vaccine to 33% (27% to 39%) at 27-30 weeks after the second dose. In the same time intervals, vaccine effectiveness against severe covid-19 also decreased (P<0.001), although to a lesser extent, from 96% (95% to 97%) to 80% (76% to 83%). High risk people (vaccine effectiveness −6%, −28% to 12%), those aged ≥80 years (11%, −15% to 31%), and those aged 60-79 years (2%, −11% to 14%) did not seem to be protected against infection at 27-30 weeks after the second dose of vaccine.

**Conclusions** The results support the vaccination campaigns targeting high risk people, those aged ≥60 years, and healthcare workers to receive a booster dose of vaccine six months after the primary vaccination cycle. The results also suggest that timing the booster dose earlier than six months after the primary vaccination cycle and extending the offer of the booster dose to the wider eligible population might be warranted.

Full article: [Effectiveness of mRNA vaccines and waning of protection against SARS-CoV-2 infection and severe covid-19 during predominant circulation of the delta variant in Italy: retrospective cohort study | The BMJ](https://www.bmj.com/content/376/bmj-2021-069052)

**Title:** The UK is an international outlier in its approach to covid in children

bmj| 9th February

Recent declines in the overall rates of covid-19 in the UK have masked the rapid and steep rise in cases among children. As of 26 January 2022, Office for National Statistics data suggest that nearly 12% of children in primary school and below (ages 2 to 11), and 6.5% of children in secondary school (ages 11 to 16), tested positive for covid-19.1

Early warnings that a lack of protections for children would lead to a wave of infections from the delta variant, causing disruption to education in the autumn term, were not heeded.2 The warnings were reiterated with omicron in December, but again, very little was done to make schools safer.3 When schools returned in January 2022, secondary school children (but not primary) were required to wear masks in school. Students in secondary schools (but not primary) were also asked to take a rapid antigen test twice a week at home and to isolate if positive. Children who were contacts of new cases (even household members) were not required to isolate. By the end of January all mask requirements in schools had been dropped and masks were actively discouraged. Just over half of 12-15 year olds had received one dose of vaccine and 5 to 11 year olds were not in general eligible for a vaccine. Carbon dioxide sensors have been distributed to assess ventilation, with advice on ventilation, and 7000 air cleaning filtration units have been made available for the worst ventilated classrooms, but it’s clear that classroom ventilation is not enough to stop omicron tearing through schools.

Although children are at much lower risk of experiencing severe illness from covid compared to (particularly older) adults, there are still a number of harms that come from attempting to “live with” high rates of infection in schools. These include record numbers of hospital admissions in children with covid, increasing rates of long covid in children, educational disruption (very high pupil and teacher absenteeism related to infection), and disruption to other sectors (e.g. parents having to stay home from work to care for children who test positive or becoming infected themselves).456

We have a much better idea now about what works to keep schools open and transmission lower: a combination of vaccination, clean indoor air, testing, contact tracing, isolation and face masks. The problem is that, particularly as far as vaccination and clean air are concerned, we are still yet to see these protections properly put in place for children.

Full opinion article: [The UK is an international outlier in its approach to covid in children | The BMJ](https://www.bmj.com/content/376/bmj.o327)

**Title:** Comparison of SARS-CoV-2 anti-spike receptor binding domain IgG antibody responses after CoronaVac, BNT162b2, ChAdOx1 COVID-19 vaccines, and a single booster dose: a prospective, longitudinal population-based study

the lancet microbe| 9th February

Background

Vaccination is an efficient strategy to control the COVID-19 pandemic. In north Cyprus, vaccine distribution started with CoronaVac followed by BNT162b2, and ChAdOx1 vaccines. An option to obtain a third booster dose with BNT162b2 or CoronaVac was later offered to people fully inoculated with CoronaVac. There are few simultaneous and comparative real-world antibody data for these three vaccines as well as boosters after CoronaVac vaccination. Our study was aimed at evaluating antibody responses after these vaccination schemes.

Methods

We did a prospective, longitudinal population-based study to measure SARS-CoV-2 anti-spike receptor binding domain (RBD) IgG concentrations, assessed by assaying blood samples collected, in participants in north Cyprus who had received the BNT162b2, ChAdOx1, or CoronaVac vaccine at 1 month and 3 months after the second dose. Participants were recruited when they voluntarily came to the laboratory for testing after vaccination, solicited from health-care access points, or from the general population. We also evaluated antibody responses 1 month after a booster dose of BNT162b2 or CoronaVac after primary CoronaVac regimen. Demographics, baseline characteristics, vaccination reactions, and percentage of antibody responders were collected by phone interviews or directly from the laboratory summarised by vaccine and age group. Antibody levels were compared between groups over time by parametric and non-parametric methods.

Findings

Recruitment, follow-up, and data collection was done between March 1 and Sept 30, 2021. BNT162b2 induced the highest seropositivity and anti-spike RBD IgG antibody titres, followed by ChAdOx1, and then by CoronaVac. In addition, the rate of decline of antibodies was fastest with CoronaVac, followed by ChAdOx1, and then by BNT162b2. For the older age group, the rate of seropositivity at 3 months after the second dose was 100% for BNT162b2, 90% for ChAdOx1, and 60% for CoronaVac. In the multivariate repeated measures model, lower antibody titres were also significantly associated with male sex, older age, and time since vaccination. Boosting a two-dose CoronaVac regimen at 6 months with a single BNT162b2 dose led to significantly increased titres of IgG compared with boosting with CoronaVac; for the 60 years and older age group, the geometric mean fold rise in antibody titre after the booster relative to 1 month post-baseline was 7·9 (95% CI 5·8–10·8) in the BNT162b2 boost group versus 2·8 (1·6–5·0) in the CoronaVac group.

Interpretation

These longitudinal data can help shape vaccination strategies. Given the low antibody titres and fast decline in the CoronaVac group in individuals 60 years or older, more potent vaccine options could be considered as the primary vaccination or booster dose in these high-risk populations to sustain antibody responses for longer.

Full article: [Comparison of SARS-CoV-2 anti-spike receptor binding domain IgG antibody responses after CoronaVac, BNT162b2, ChAdOx1 COVID-19 vaccines, and a single booster dose: a prospective, longitudinal population-based study - The Lancet Microbe](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247%2821%2900305-0/fulltext)

**Title:** Safety and immunogenicity of two recombinant DNA COVID-19 vaccines containing the coding regions of the spike or spike and nucleocapsid proteins: an interim analysis of two open-label, non-randomised, phase 1 trials in healthy adults

the lancet microbe| 8th February

Background

We assessed the safety and immunogenicity of two recombinant DNA vaccines for COVID-19: GX-19 containing plasmid DNA encoding the SARS-CoV-2 spike protein, and GX-19N containing plasmid DNA encoding the SARS-CoV-2 receptor-binding domain (RBD) foldon, nucleocapsid protein, and plasmid DNA encoding the spike protein.

Methods

Two open-label non-randomised phase 1 trials, one of GX-19 and the other of GX-19N were done at two hospitals in South Korea. We enrolled healthy adults aged 19–49 years for the GX-19 trial and healthy adults aged 19–54 years for the GX-19N trial. Participants who tested positive by serological testing for SARS-CoV-2 were excluded. At 4-week intervals, the GX-19 trial participants received two vaccine doses (either 1·5 mg or 3·0 mg), and the GX-19N trial participants received two 3·0 mg doses. The vaccines were delivered intramuscularly using an electroporator. The participants were followed up for 52 weeks after first vaccination. Data collected up to day 57 after first vaccination were analysed in this interim analysis. The primary outcome was safety within 28 days after each vaccination measured in the intention-to-treat population. The secondary outcome was vaccine immunogenicity using blood samples collected on day 43 or 57 after first vaccination measured in the intention-to-treat population. The GX-19 ([NCT044445389](http://clinicaltrials.gov/show/NCT044445389)) and GX-19N ([NCT04715997](http://clinicaltrials.gov/show/NCT04715997)) trials are registered with [ClinicalTrials.gov](http://clinicaltrials.gov/).

Findings

Between June 17 and July 30, 2020, we screened 97 individuals, of whom 40 (41%) participants were enrolled in the GX-19 trial (20 [50%] in the 1·5 mg group and 20 [50%] in the 3·0 mg group). Between Dec 28 and 31, 2020, we screened 23 participants, of whom 21 (91%) participants were enrolled on the GX-19N trial. 32 (52%) of 61 participants reported 80 treatment-emergent adverse events after vaccination. All solicited adverse events were mild except one (2%) case of moderate fatigue in the 1·5 mg GX-19 group; no serious vaccine-related adverse events were detected. Binding antibody responses increased after second dose of vaccination in all groups (p=0·0002 in the 1·5 mg GX-19 group; p<0·0001 in the 3·0 mg GX-19; and p=0·0004 for the spike protein and p=0·0001 for the RBD in the 3·0 mg GX-19N group).

Interpretation

GX-19 and GX-19N are safe and well tolerated. GX-19N induces humoral and broad SARS-CoV-2-specific T-cell responses. GX-19N shows lower neutralising antibody responses and needs improvement to enhance immunogenicity.

Full article: [Safety and immunogenicity of two recombinant DNA COVID-19 vaccines containing the coding regions of the spike or spike and nucleocapsid proteins: an interim analysis of two open-label, non-randomised, phase 1 trials in healthy adults - The Lancet Microbe](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247%2821%2900358-X/fulltext)

**Title:** Final Analysis of Efficacy and Safety of Single-Dose Ad26.COV2.S

jama| 9th February

**BACKGROUND**

The Ad26.COV2.S vaccine was highly effective against severe–critical coronavirus disease 2019 (Covid-19), hospitalization, and death in the primary phase 3 efficacy analysis.

**METHODS**

We conducted the final analysis in the double-blind phase of our multinational, randomized, placebo-controlled trial, in which adults were assigned in a 1:1 ratio to receive single-dose Ad26.COV2.S (5×1010 viral particles) or placebo. The primary end points were vaccine efficacy against moderate to severe–critical Covid-19 with onset at least 14 days after administration and at least 28 days after administration in the per-protocol population. Safety and key secondary and exploratory end points were also assessed.

**RESULTS**

Median follow-up in this analysis was 4 months; 8940 participants had at least 6 months of follow-up. In the per-protocol population (39,185 participants), vaccine efficacy against moderate to severe–critical Covid-19 at least 14 days after administration was 56.3% (95% confidence interval [CI], 51.3 to 60.8; 484 cases in the vaccine group vs. 1067 in the placebo group); at least 28 days after administration, vaccine efficacy was 52.9% (95% CI, 47.1 to 58.1; 433 cases in the vaccine group vs. 883 in the placebo group). Efficacy in the United States, primarily against the reference strain (B.1.D614G) and the B.1.1.7 (alpha) variant, was 69.7% (95% CI, 60.7 to 76.9); efficacy was reduced elsewhere against the P.1 (gamma), C.37 (lambda), and B.1.621 (mu) variants. Efficacy was 74.6% (95% CI, 64.7 to 82.1) against severe–critical Covid-19 (with only 4 severe–critical cases caused by the B.1.617.2 [delta] variant), 75.6% (95% CI, 54.3 to 88.0) against Covid-19 leading to medical intervention (including hospitalization), and 82.8% (95% CI, 40.5 to 96.8) against Covid-19–related death, with protection lasting 6 months or longer. Efficacy against any severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was 41.7% (95% CI, 36.3 to 46.7). Ad26.COV2.S was associated with mainly mild-to-moderate adverse events, and no new safety concerns were identified.

**CONCLUSIONS**

A single dose of Ad26.COV2.S provided 52.9% protection against moderate to severe–critical Covid-19. Protection varied according to variant; higher protection was observed against severe Covid-19, medical intervention, and death than against other end points and lasted for 6 months or longer. (Funded by Janssen Research and Development and others; ENSEMBLE ClinicalTrials.gov number, [**NCT04505722. opens in new tab**](http://clinicaltrials.gov/show/NCT04505722).)

Full article: [Final Analysis of Efficacy and Safety of Single-Dose Ad26.COV2.S | NEJM](https://www.nejm.org/doi/full/10.1056/NEJMoa2117608?query=featured_coronavirus)

**Title:** Efficacy and Safety of NVX-CoV2373 in Adults in the United States and Mexico

NEJM| 10th February

**BACKGROUND**

NVX-CoV2373 is an adjuvanted, recombinant spike protein nanoparticle vaccine that was shown to have clinical efficacy for the prevention of coronavirus disease 2019 (Covid-19) in phase 2b–3 trials in the United Kingdom and South Africa, but its efficacy had not yet been tested in North America.

**METHODS**

We conducted a phase 3, randomized, observer-blinded, placebo-controlled trial in the United States and Mexico during the first half of 2021 to evaluate the efficacy and safety of NVX-CoV2373 in adults (≥18 years of age) who had not had severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Participants were randomly assigned in a 2:1 ratio to receive two doses of NVX-CoV2373 or placebo 21 days apart. The primary objective was to determine vaccine efficacy against reverse-transcriptase–polymerase-chain-reaction–confirmed Covid-19 occurring at least 7 days after the second dose. Vaccine efficacy against moderate-to-severe disease and against different variants was also assessed.

**RESULTS**

Of the 29,949 participants who underwent randomization between December 27, 2020, and February 18, 2021, a total of 29,582 (median age, 47 years; 12.6% ≥65 years of age) received at least one dose: 19,714 received vaccine and 9868 placebo. Over a period of 3 months, 77 cases of Covid-19 were noted — 14 among vaccine recipients and 63 among placebo recipients (vaccine efficacy, 90.4%; 95% confidence interval [CI], 82.9 to 94.6; P<0.001). Ten moderate and 4 severe cases occurred, all in placebo recipients, yielding vaccine efficacy against moderate-to-severe disease of 100% (95% CI, 87.0 to 100). Most sequenced viral genomes (48 of 61, 79%) were variants of concern or interest — largely B.1.1.7 (alpha) (31 of the 35 genomes for variants of concern, 89%). Vaccine efficacy against any variant of concern or interest was 92.6% (95% CI, 83.6 to 96.7). Reactogenicity was mostly mild to moderate and transient but was more frequent among NVX-CoV2373 recipients than among placebo recipients and was more frequent after the second dose than after the first dose.

**CONCLUSIONS**

NVX-CoV2373 was safe and effective for the prevention of Covid-19. Most breakthrough cases were caused by contemporary variant strains. (Funded by Novavax and others; PREVENT-19 ClinicalTrials.gov number, [**NCT04611802. opens in new tab**](http://clinicaltrials.gov/show/NCT04611802).)

Full article: [Efficacy and Safety of NVX-CoV2373 in Adults in the United States and Mexico | NEJM](https://www.nejm.org/doi/full/10.1056/NEJMoa2116185)

**Title:** Analysis of COVID-19 Risk Following a Ring Vaccination Intervention to Address SARS-CoV-2 Alpha Variant Transmission in Montreal, Canada

jama network open| 11th february

**Question**  Is ring vaccination targeting contacts of confirmed cases and persons who are in close contact with these contacts useful for controlling local SARS-CoV-2 transmission following the introduction of a new variant?

**Findings**  In this cohort study of 106 Montreal neighborhoods, ring vaccination was associated with a reduction in COVID-19 incidence in areas with high SARS-CoV-2 Alpha variant case counts.

**Meaning**  These results suggest that ring vaccination may be considered an adjunct to mass immunization to control transmission in specific areas where new variants are first introduced, based on local epidemiology.

Full article: [Analysis of COVID-19 Risk Following a Ring Vaccination Intervention to Address SARS-CoV-2 Alpha Variant Transmission in Montreal, Canada | Vaccination | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788978)

**Title:** Association of COVID-19 Incidence and Mortality Rates With School Reopening in Brazil During the COVID-19 Pandemic

JAMA Health forum| 11th February

**Question**  Is the reopening of schools during the COVID-19 pandemic associated with increased COVID-19 incidence and mortality?

**Findings**  In this cross-sectional study of 643 Brazilian municipalities including 18 761 schools, on average, there was no systematic association between school reopening and COVID-19 incidence or mortality in São Paulo State up to 12 weeks after reopening, which was also the case for schools in the most vulnerable conditions. Aggregate mobility was already high before the school reopening and did not significantly increase afterwards.

**Meaning**  The results of this study suggest that reopening schools under appropriate protocols in low- and middle-income countries during the pandemic is unlikely to be associated with higher aggregate COVID-19 cases or deaths when counterfactual mobility is already high.

Full article: [JAMA Health Forum – Health Policy, Health Care Reform, Health Affairs | JAMA Health Forum | JAMA Network](https://jamanetwork.com/journals/jama-health-forum/fullarticle/2788936)

**Title:** Association of BNT162b2 COVID-19 Vaccination During Pregnancy With Neonatal and Early Infant Outcomes

jama pediatrics| 10th february

**Questions**  Is prenatal exposure to maternal BNT162b2 messenger RNA COVID-19 vaccine associated with adverse outcomes at birth or early childhood?

**Findings**  In a population-based study including 24 288 singleton live births, the risks of preterm birth and small birth weight were similar between newborns prenatally exposed and unexposed to maternal vaccination.

**Meaning**  Maternal BNT162b2 vaccination in pregnancy was not associated with detrimental outcomes to the offspring.

Full article: [Association of BNT162b2 COVID-19 Vaccination During Pregnancy With Neonatal and Early Infant Outcomes | Neonatology | JAMA Pediatrics | JAMA Network](https://jamanetwork.com/journals/jamapediatrics/fullarticle/2788938)

**Title:** Comparison of SARS-CoV-2 Test Positivity in NCAA Division I Student Athletes vs Nonathletes at 12 Institutions

jama network open| 9th february

**Question**  Was participation in collegiate athletics associated with increased SARS-CoV-2 test positivity?

**Findings**  In this cross-sectional study using data for 555 372 student athlete and 3 482 845 nonathlete student SARS-CoV-2 tests reported from 12 National Collegiate Athletic Association Division I institutions, participation in collegiate athletics was not associated with increased test positivity in student athletes compared with nonathlete students.

**Meaning**  This finding suggests that collegiate athletics may be held safely in the COVID-19 pandemic without associated increases in test positivity among student athletes.

Full article: [Comparison of SARS-CoV-2 Test Positivity in NCAA Division I Student Athletes vs Nonathletes at 12 Institutions | Adolescent Medicine | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788852)

Commentary: [College Athletic Programs Thwart the Spread of SARS-CoV-2 During the COVID-19 Pandemic | Adolescent Medicine | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788859)

**workforce wellbeing**

**Title:** England’s U turn on covid-19 vaccine mandate for NHS staff

bmj| 10th February

An avoidable and costly episode that raises concerning questions about governance

Two years into a pandemic, with hopes of respite for exhausted healthcare workers repeatedly shattered by the emergence of new SARS-CoV-2 variants, those in charge in the NHS just want certainty. So it is little wonder that, over the past few weeks, they have become increasingly frustrated as they struggle to interpret the government’s changing intentions for vaccination of their staff. But when this is over we should all reflect on what this episode says about how the country is being run.

Full editorial: [England’s U turn on covid-19 vaccine mandate for NHS staff | The BMJ](https://www.bmj.com/content/376/bmj.o353)

**Title:** Covid-19: Solely refusing vaccine will not trigger a fitness to practise investigation, says GMC

bmj| 11th February

The General Medical Council (GMC) does not consider refusal of covid-19 vaccine to be a sufficient reason for launching a fitness to practise investigation, the regulator has said in a joint statement with the Academy of Medical Royal Colleges.[**1**](https://www.bmj.com/content/376/bmj.o372#ref-1)

Issued on 10 February, the statement follows the government’s last minute U turn on a plan to make covid-19 vaccination mandatory for NHS staff in England—a move that health leaders had warned would further exacerbate the staffing crisis in the NHS.[**2**](https://www.bmj.com/content/376/bmj.o372#ref-2)

But the statement said that “while the GMC does not consider that solely turning down vaccination would in itself form the basis of a fitness to practise referral, doctors have a professional duty to protect patients from risks posed by their health, and to be immunised against common serious communicable diseases, unless contraindicated.”

Full news article: [Covid-19: Solely refusing vaccine will not trigger a fitness to practise investigation, says GMC | The BMJ](https://www.bmj.com/content/376/bmj.o372)

**Title:** Covid-19: Staff absences are continuing to stretch NHS hospitals, say leaders

bmj| 11th february

Staff absences due to covid-19 are continuing to place acute hospital services under major pressure, medical leaders have told *The BMJ*.

Official data show that an average of 70 000 hospital trust staff in England were absent from work in the week ending 30 January, 28 000 (40%) of whom were off because of covid-19.[**1**](https://www.bmj.com/content/376/bmj.o350#ref-1) On 18 and 19 January *The BMJ* visited University Hospitals Coventry and Warwickshire NHS Trust (UHCW) to speak to leaders and staff about workforce pressures ([**video 1**](https://www.bmj.com/content/376/bmj.o350#media-1)).

Full news article: [Covid-19: Staff absences are continuing to stretch NHS hospitals, say leaders | The BMJ](https://www.bmj.com/content/376/bmj.o350)

**Title:** Covid-19: Medical regulators should ensure that health workers are vaccinated, says Javid

bmj| 8th February

England’s health secretary has urged medical regulators to send a “clear message” to healthcare workers that they should be vaccinated against covid-19, despite the government dropping its legal vaccine mandate for NHS staff in England.[**1**](https://www.bmj.com/content/376/bmj.o346#ref-1)

Last week’s last minute U turn on mandatory vaccination was welcomed by medical bodies, which had warned that forcing staff to be vaccinated or face dismissal would worsen chronic workforce shortages in the NHS. On 16 January 80 092 staff (5.4% of the total) still remained unvaccinated.

But in a letter to nine healthcare regulators including the General Medical Council and Nursing and Midwifery Council seen by the *Times* newspaper,[**2**](https://www.bmj.com/content/376/bmj.o346#ref-2) Sajid Javid said that the government’s last minute decision to abandon compulsory vaccines “in no way diminishes the importance that health and care workers are vaccinated.”

Full news article: [Covid-19: Medical regulators should ensure that health workers are vaccinated, says Javid | The BMJ](https://www.bmj.com/content/376/bmj.o346)

**other**

**Title:** Covid-19: What do we know about omicron sublineages?

BMJ| 11th February

On 26 November 2021 WHO designated omicron a variant of concern. With its sublineage BA.2 now widespread, **Elisabeth Mahase** looks at what science has found out about the variant and its three (so far) variations

Full article: [Covid-19: What do we know about omicron sublineages? | The BMJ](https://www.bmj.com/content/376/bmj.o358)

**Title:** Covid-19: Government plans to remove all remaining restrictions in England a month early

BMJ| 9th February

The government plans to end all remaining covid restrictions in England—including the legal obligation to self-isolate—ahead of schedule later this month, the prime minister, Boris Johnson, has said.

The current restrictions, including the requirement that anyone who tests positive for covid-19 must self-isolate for at least five days, are due to expire on 24 March. But Johnson, addressing MPs during prime minister’s questions on 9 February, said that the remaining rules could end early if recent trends in the data continued.

“It is my intention to return on the first day after the half term recess to present our strategy for living with covid,” he said. “Provided the current encouraging trends in the data continue, it is my expectation that we will be able to end the last domestic restrictions—including the legal requirement to self-isolate if you test positive—a full month early.”

If the government proceeds with its full removal of restrictions the law will be replaced by guidance that people should stay at home if they have covid, said Downing Street after Johnson’s announcement, adding that fresh guidance on living with covid would include a decision on whether travel restrictions will remain until the end of March.

Full news article: [Covid-19: Government plans to remove all remaining restrictions in England a month early | The BMJ](https://www.bmj.com/content/376/bmj.o355)

**Title:** Covid-19: Ottawa declares emergency as truckers’ protest continues

bmj| 9th February

Canada’s capital, Ottawa, has declared a state of emergency in response to a protest against pandemic health measures that has brought the city centre to a near standstill and shows no sign of ending after 12 days.

Full news article: [Covid-19: Ottawa declares emergency as truckers’ protest continues | The BMJ](https://www.bmj.com/content/376/bmj.o352)

**Title:** Multivariate, Transgenerational Associations of the COVID-19 Pandemic Across Minoritized and Marginalized Communities

jama Psychiatry| 9th february

**Question**  What baseline pre–COVID-19 pandemic household factors are associated with COVID-19 experiences as reported by approximately 10 000 children and their parents?

**Findings**  In this study of 9267 youth-parent dyads, of more than 17 000 variables, social determinants of inequity, including household income and family structure, emerged as the primary correlates of negative COVID-19 experiences, including increased difficulties with school among children and concerns over racism associated with the COVID-19 pandemic among parents.

**Meaning**  Community-level, transgenerational intervention strategies may be needed to combat the disproportionate burden of pandemics on minoritized and marginalized racial and ethnic populations.

Full article: [Multivariate, Transgenerational Associations of the COVID-19 Pandemic Across Minoritized and Marginalized Communities | Adolescent Medicine | JAMA Psychiatry | JAMA Network](https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2788897)

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