COVID-19 weekly update

January 31st 2022

clinical management

**Title:** Covid-19: Antibody “signature” could predict risk of long covid

BMJ| 28th JANUARY

Researchers have identified an immunoglobulin “signature” that could be used to predict which patients are most at risk of developing post-acute covid syndrome (PACS), otherwise known as long covid.

In a multicentre prospective study, 175 patients with covid-19 and 40 healthy control group participants were followed for up to a year. More than half of the patients with covid reported long covid symptoms lasting longer than a month. Those who developed long covid were found to have lower levels of IgM and IgG3 antibodies than those who quickly recovered, found the research, published in *Nature Communications*.[**1**](https://www.bmj.com/content/376/bmj.o245#ref-1) A history of asthma was also highly associated with PACS, the study found.

The researchers combined data on immunoglobulin concentrations with a patient’s age, history of asthma, and five symptoms during the primary infection to develop a PACS score that could predict the risk of developing long term illness. The PACS score was then validated in an independent group of 395 people with covid-19.

The researchers, from the University of Zurich, said that the score might be especially helpful in hospital settings for early identification of those patients at a very high risk of developing PACS. It could also allow the study of targeted preventive treatments such as inhaled corticosteroids or intravenous immunoglobulin treatments.

The researchers said more research was still needed but that a PACS score or long covid risk calculator would be available soon at pacs-score.com.

Full news article: [Covid-19: Antibody “signature” could predict risk of long covid | The BMJ](https://www.bmj.com/content/376/bmj.o245)

**Title:** Gout and the risk of COVID-19 diagnosis and death in the UK Biobank: a population-based study

The lancet – rheumatology| 28th January

Background

There is a paucity of data on outcomes for people with gout and COVID-19. We aimed to assess whether gout is a risk factor for diagnosis of COVID-19 and COVID-19-related death, and to test for sex- and drug-specific differences in risk.

Methods

We used data from the UK Biobank, which included 15 871 people with gout. We used multivariable-adjusted logistic regression in the following analyses using a case-control study design: to test for an association between gout and COVID-19 diagnosis in the entire UK Biobank cohort (n=459 837); to test for an association between gout and COVID-19-related death in people who were known to have died or survived with COVID-19 (n=15 772); to test for an association between gout and COVID-19-related death in the entire UK Biobank cohort (n=459 837); and to assess risk of COVID-19-related death in a subset of patients from the UK Biobank cohort with prescription data, stratified by prescription of urate-lowering therapy and colchicine (n=341 398). Models 1 and 2 were adjusted for age group, sex, ethnicity, Townsend deprivation index, BMI, and smoking status. Model 2 was also adjusted for diagnosis of 16 other diseases that are established comorbidities of gout or established risk factors for COVID-19-related death.

Findings

Gout was associated with diagnosis of COVID-19 (odds ratio [OR] 1·20, 95% CI 1·11–1·29) but not with risk of COVID-19-related death in the cohort of patients diagnosed with COVID-19 (1·20, 0·96–1·51). In the entire cohort, gout was associated with COVID-19-related death (1·29, 1·06–1·56); women with gout had an increased risk of COVID-19-related death (1·98, 1·34–2·94), whereas men with gout did not (1·16, 0·93–1·45). We found no significant differences in the risk of COVID-19-related death according to prescription of urate-lowering therapy or colchicine. When patients with gout were stratified by vaccination status, the risk of diagnosis with COVID-19 was significant in the non-vaccinated group (1·21, 1·11–1·30) but not the vaccinated group (1·09, 0·65–1·85).

Interpretation

Gout is a risk factor for COVID-19-related death in the UK Biobank cohort, with an increased risk in women with gout, which was driven by risk factors independent of the metabolic comorbidities of gout.

Full article: [Gout and the risk of COVID-19 diagnosis and death in the UK Biobank: a population-based study - The Lancet Rheumatology](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00401-X/fulltext)

**Title:** Hyperimmune immunoglobulin for hospitalised patients with COVID-19 (ITAC): a double-blind, placebo-controlled, phase 3, randomised trial

the lancet| 27th january

Background

Passive immunotherapy using hyperimmune intravenous immunoglobulin (hIVIG) to SARS-CoV-2, derived from recovered donors, is a potential rapidly available, specific therapy for an outbreak infection such as SARS-CoV-2. Findings from randomised clinical trials of hIVIG for the treatment of COVID-19 are limited.

Methods

In this international randomised, double-blind, placebo-controlled trial, hospitalised patients with COVID-19 who had been symptomatic for up to 12 days and did not have acute end-organ failure were randomly assigned (1:1) to receive either hIVIG or an equivalent volume of saline as placebo, in addition to remdesivir, when not contraindicated, and other standard clinical care. Randomisation was stratified by site pharmacy; schedules were prepared using a mass-weighted urn design. Infusions were prepared and masked by trial pharmacists; all other investigators, research staff, and trial participants were masked to group allocation. Follow-up was for 28 days. The primary outcome was measured at day 7 by a seven-category ordinal endpoint that considered pulmonary status and extrapulmonary complications and ranged from no limiting symptoms to death. Deaths and adverse events, including organ failure and serious infections, were used to define composite safety outcomes at days 7 and 28. Prespecified subgroup analyses were carried out for efficacy and safety outcomes by duration of symptoms, the presence of anti-spike neutralising antibodies, and other baseline factors. Analyses were done on a modified intention-to-treat (mITT) population, which included all randomly assigned participants who met eligibility criteria and received all or part of the assigned study product infusion. This study is registered with [ClinicalTrials.gov](http://clinicaltrials.gov/), [NCT04546581](http://clinicaltrials.gov/show/NCT04546581).

Findings

From Oct 8, 2020, to Feb 10, 2021, 593 participants (n=301 hIVIG, n=292 placebo) were enrolled at 63 sites in 11 countries; 579 patients were included in the mITT analysis. Compared with placebo, the hIVIG group did not have significantly greater odds of a more favourable outcome at day 7; the adjusted OR was 1·06 (95% CI 0·77–1·45; p=0·72). Infusions were well tolerated, although infusion reactions were more common in the hIVIG group (18·6% *vs* 9·5% for placebo; p=0·002). The percentage with the composite safety outcome at day 7 was similar for the hIVIG (24%) and placebo groups (25%; OR 0·98, 95% CI 0·66–1·46; p=0·91). The ORs for the day 7 ordinal outcome did not vary for subgroups considered, but there was evidence of heterogeneity of the treatment effect for the day 7 composite safety outcome: risk was greater for hIVIG compared with placebo for patients who were antibody positive (OR 2·21, 95% CI 1·14–4·29); for patients who were antibody negative, the OR was 0·51 (0·29–0·90; pinteraction=0·001).

Interpretation

When administered with standard of care including remdesivir, SARS-CoV-2 hIVIG did not demonstrate efficacy among patients hospitalised with COVID-19 without end-organ failure. The safety of hIVIG might vary by the presence of endogenous neutralising antibodies at entry.

Full article: [Hyperimmune immunoglobulin for hospitalised patients with COVID-19 (ITAC): a double-blind, placebo-controlled, phase 3, randomised trial - The Lancet](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00101-5/fulltext)

**Title:** The emergence of COVID-19 associated mucormycosis: a review of cases from 18 countries

THE LANCET MICROBE| 25th JANUARY

Reports of COVID-19-associated mucormycosis have been increasing in frequency since early 2021, particularly among patients with uncontrolled diabetes. Patients with diabetes and hyperglycaemia often have an inflammatory state that could be potentiated by the activation of antiviral immunity to SARS-CoV2, which might favour secondary infections. In this Review, we analysed 80 published and unpublished cases of COVID-19-associated mucormycosis. Uncontrolled diabetes, as well as systemic corticosteroid treatment, were present in most patients with COVID-19-associated mucormycosis, and rhino-orbital cerebral mucormycosis was the most frequent disease. Mortality was high at 49%, which was particularly due to patients with pulmonary or disseminated mucormycosis or cerebral involvement. Furthermore, a substantial proportion of patients who survived had life-changing morbidities (eg, loss of vision in 46% of survivors). Our Review indicates that COVID-19-associated mucormycosis is associated with high morbidity and mortality. Diagnosis of pulmonary mucormycosis is particularly challenging, and might be frequently missed in India.

Full article: [The emergence of COVID-19 associated mucormycosis: a review of cases from 18 countries - The Lancet Microbe](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00237-8/fulltext)

**Title:** Clinical Characteristics and Outcomes of Patients With COVID-19–Associated Acute Respiratory Distress Syndrome Who Underwent Lung Transplant

jama| 27th January

**Question**  What were the clinical outcomes of patients who underwent a lung transplant after developing COVID-19–associated acute respiratory distress syndrome (ARDS) at a single center in the US?

**Findings**  In this retrospective case series involving 102 consecutive patients who underwent a lung transplant between January 21, 2020, and September 30, 2021, at a single center in Chicago, Illinois, patient survival was 100% for the 30 patients who had COVID-19–associated ARDS and 83% for the 72 patients without COVID-19, as of November 15, 2021.

**Meaning**  In this case series of patients who underwent a lung transplant, survival was 100% in patients who had COVID-19–associated ARDS as of November 15, 2021.

Full article: [Clinical Characteristics and Outcomes of Patients With COVID-19–Associated Acute Respiratory Distress Syndrome Who Underwent Lung Transplant | Cardiothoracic Surgery | JAMA | JAMA Network](https://jamanetwork.com/journals/jama/fullarticle/2788640)

**Title:** Effect of Noninvasive Respiratory Strategies on Intubation or Mortality Among Patients With Acute Hypoxemic Respiratory Failure and COVID-19

jama| 24th January

**Question**  What is the effect of initial noninvasive respiratory strategies using continuous positive airway pressure (CPAP) or high-flow nasal oxygen (HFNO), compared with an initial strategy of conventional oxygen therapy, on the risk of tracheal intubation or mortality among hospitalized adults with acute hypoxemic respiratory failure due to COVID-19?

**Findings**  In this randomized clinical trial of 1273 patients, the composite primary outcome of tracheal intubation or mortality within 30 days occurred in 36% of the patients in the CPAP group compared with 44% in the conventional oxygen therapy group, a difference that was statistically significant, and occurred in 44% in the HFNO group compared with 45% in the conventional oxygen therapy group, a difference that was not significantly different.

**Meaning**  Among patients with acute hypoxemic respiratory failure and COVID-19, an initial strategy of CPAP significantly reduced the risk of tracheal intubation or mortality compared with conventional oxygen therapy, but there was no significant difference between an initial strategy of HFNO compared with conventional oxygen therapy.

Full article: [Effect of Noninvasive Respiratory Strategies on Intubation or Mortality Among Patients With Acute Hypoxemic Respiratory Failure and COVID-19: The RECOVERY-RS Randomized Clinical Trial | Critical Care Medicine | JAMA | JAMA Network](https://jamanetwork.com/journals/jama/fullarticle/2788505)

**Title:** APOL1 Risk Variants, Acute Kidney Injury, and Death in Participants With African Ancestry Hospitalized With COVID-19 From the Million Veteran Program

JAMA INTERN MED| 28th January

**Question**  Are *APOL1* high-risk genotypes observed in individuals with African ancestry associated with acute kidney injury (AKI) and death following hospitalization for COVID-19?

**Findings**  In this cohort of 990 veterans with African ancestry hospitalized with COVID-19, 1 in 8 had *APOL1* high-risk genotypes. Of those with high-risk genotypes, 51.2% had AKI, and 19.2% died, suggesting that high-risk genotype may be associated with a 2-fold increase in the odds of severe AKI and death; this increased risk was observed even in patients with normal kidney function prior to COVID-19.

**Meaning**  *APOL1* high-risk genotypes were associated with increased odds of AKI, AKI severity, and death in individuals with African ancestry hospitalized with COVID-19.

Full article: [APOL1 Risk Variants, Acute Kidney Injury, and Death in Participants With African Ancestry Hospitalized With COVID-19 From the Million Veteran Program | Acute Kidney Injury | JAMA Internal Medicine | JAMA Network](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2788707)

**Title:** Association of Convalescent Plasma Treatment With Clinical Status in Patients Hospitalized With COVID-19

Jama network open|25th january

**Question**  What is the pooled evidence from high-quality randomized clinical trials regarding the safety and potential benefit of convalescent plasma to treat hospitalized patients with COVID-19?

**Findings**  In this meta-analysis of 8 randomized clinical trials enrolling 2341 participants, individual patient data were monitored in real time and analyzed using a robust bayesian framework and advanced statistical modeling. No association of convalescent plasma with clinical outcomes was found.

**Meaning**  These findings suggest that real-time individual patient data pooling and meta-analysis during a pandemic are feasible, offering a model for future research and providing a rich data resource.

Full article: [Association of Convalescent Plasma Treatment With Clinical Status in Patients Hospitalized With COVID-19: A Meta-analysis | Infectious Diseases | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788377)

**Title:** Development and Validation of a Treatment Benefit Index to Identify Hospitalized Patients With COVID-19 Who May Benefit From Convalescent Plasma

jama network open| 25th january

**Question**  What patient characteristics are associated with benefit from treatment with COVID-19 convalescent plasma (CCP)?

**Findings**  This prognostic study of 2287 patients hospitalized with COVID-19 identified a combination of baseline characteristics that predict a gradation of benefit from CCP compared with treatment without CCP. Preexisting health conditions (diabetes, cardiovascular and pulmonary diseases), blood type A or AB, and earlier stage of COVID-19 were associated with a larger treatment benefit.

**Meaning**  These findings suggest that simple patient information collected at hospitalization can be used to guide CCP treatment decisions for patients with COVID-19.

Full reference: [Development and Validation of a Treatment Benefit Index to Identify Hospitalized Patients With COVID-19 Who May Benefit From Convalescent Plasma | Infectious Diseases | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788376)

**Title:** Tixagevimab and Cilgavimab (Evusheld) for Pre-Exposure Prophylaxis of COVID-19

JAMA| 25th january

The FDA has issued an Emergency Use Authorization (EUA) for the investigational long-acting monoclonal antibodies tixagevimab and cilgavimab (Evusheld – AstraZeneca) to be administered concomitantly by IM injection for pre-exposure prophylaxis of COVID-19 in persons ≥12 years old who weigh ≥40 kg and have either a history of severe allergy that prevents their vaccination against COVID-19 or moderate or severe immune compromise (see [Box](https://jamanetwork.com/journals/jama/fullarticle/2788354#jml210005b1)). They are the first drugs to be authorized by the FDA for this indication.[1](https://jamanetwork.com/journals/jama/fullarticle/2788354#jml210005r1) Two other pairs of antibodies, bamlanivimab plus etesevimab (Lilly) and casirivimab plus imdevimab (REGEN-COV), are authorized for post-exposure prophylaxis of COVID-19.[2](https://jamanetwork.com/journals/jama/fullarticle/2788354#jml210005r2),[3](https://jamanetwork.com/journals/jama/fullarticle/2788354#jml210005r3)

Full article: [Tixagevimab and Cilgavimab (Evusheld) for Pre-Exposure Prophylaxis of COVID-19 | Coronavirus (COVID-19) | JAMA | JAMA Network](https://jamanetwork.com/journals/jama/fullarticle/2788354)

recovery

**Title** Covid-19: Be realistic about elective recovery plan, say leaders

BMJ| 25th JANUARY

An apparent row over targets is further delaying publication of the recovery plan for elective care, amid calls for the government to be realistic, given the scale of the backlog and the continuing high incidence of omicron infections.

Almost six million people are on a hospital waiting list in England, of whom 312 665 were waiting more than a year and 1225 more than two years by the end of October.[**1**](https://www.bmj.com/content/376/bmj.o208#ref-1) The recovery plan was due to be published in December but was initially delayed when the omicron wave struck and threatened to overwhelm the NHS.

Full news article: [Covid-19: Be realistic about elective recovery plan, say leaders | The BMJ](https://www.bmj.com/content/376/bmj.o208)

**Title:** Covid-19: Europe could be headed for pandemic “endgame,” says WHO region chief

BMJ| 25th JANUARY

The rapid spread of the omicron variant of SARS-CoV-2 could see an end to the pandemic in Europe, with the variant likely to have infected 60% of people on the continent by March, the World Health Organization’s regional director for Europe has said.

“It’s plausible that the region is moving towards a kind of pandemic endgame,” Hans Kluge told Agence France-Presse on 23 January. Once the current wave subsides, he said, “there will be for some weeks and months a global immunity, either thanks to the vaccine or because people have immunity because of the infection, and also lowering seasonal risk.”

“We anticipate that there will be a period of quiet before covid-19 may come back towards the end of the year, but not necessarily the pandemic coming back,” Kluge said.

But Kluge said it is still too early to consider covid-19 endemic and warned that other variants could emerge to upset calculations. “There is a lot of talk about ‘endemic’ but endemic means that it is possible to predict what’s going to happen,” he said. “This virus has surprised us more than once.”

Given the variant’s rapid spread across Europe, Kluge said countries should focus on “minimising disruption of hospitals, schools, and the economy, and putting huge effort into protecting the vulnerable,” rather than imposing lockdowns.

Full news article: [Covid-19: Europe could be headed for pandemic “endgame,” says WHO region chief | The BMJ](https://www.bmj.com/content/376/bmj.o205)

**Title:** Clinical Outcomes Among Patients With 1-Year Survival Following Intensive Care Unit Treatment for COVID-19

JAMA| 24th January

**Question**  What are the 1-year outcomes among patients who survive intensive care unit (ICU) treatment for COVID-19?

**Findings**  In this exploratory multicenter prospective cohort study that included 246 patients who were alive 1 year following ICU treatment for COVID-19, 74.3% reported physical symptoms, 26.2% reported mental symptoms, and 16.2% reported cognitive symptoms.

**Meaning**  Physical, mental, and cognitive symptoms were frequent 1 year after ICU treatment for COVID-19.

Full article: [Clinical Outcomes Among Patients With 1-Year Survival Following Intensive Care Unit Treatment for COVID-19 | Critical Care Medicine | JAMA | JAMA Network](https://jamanetwork.com/journals/jama/fullarticle/2788504)

**Title:** COVID-19–Related Life Experiences, Outdoor Play, and Long-term Adiposity Changes Among Preschool- and School-Aged Children in Singapore 1 Year After Lockdown

jama pediatrics| 24th january

**Question**  What are typical lifestyle changes experienced by children after COVID-19–related lockdowns, and what are potential long-term outcomes?

**Findings**  In this cohort study of 604 children, one-third of parents and school-aged children reported elimination of outdoor play or exercise, and those with lower family income before and after lockdown were more likely to report elimination of outdoor play. Elimination of play was associated with increased adiposity 1 year after lockdown in school-aged children but not preschool-aged children.

**Meaning**  Outdoor play is an important part of children’s well-being, and efforts to mitigate avoidable negative outcomes of COVID-19 pandemic–related lockdowns should be considered.

Full article: [COVID-19–Related Life Experiences, Outdoor Play, and Long-term Adiposity Changes Among Preschool- and School-Aged Children in Singapore 1 Year After Lockdown | Global Health | JAMA Pediatrics | JAMA Network](https://jamanetwork.com/journals/jamapediatrics/fullarticle/2788280)

**Title:** Patient Experience Before The Omicron Wave: The Storm Before The Storm

**Patients Association| 31st January**

This report, based on a survey of more than 1,000 UK patients conducted over a month just before Christmas 2021, finds the disruption to health and care services caused by the pandemic is profound and long-term. The survey found: two out of three patients lack confidence that the health and care system will be able to deliver high quality care and treatment consistently after the pandemic; more than half had not been kept informed about what was happening with their care; one in four did not feel they had been treated with respect and another one in four reported not being listened to; half had not been able to access the services they needed; and half had struggled to get GP appointments.

* [Report](https://www.patients-association.org.uk/Handlers/Download.ashx?IDMF=4bd28e84-3adf-46b9-90d8-02b544f95277)
* [Press release](https://www.patients-association.org.uk/News/nhs-losing-patients-confidence-patients-association-survey-finds)

Infection control

**Title:** Covid-19: Cuba will request WHO approval for homegrown vaccine

bmj| 26th January

Cuban health officials have said that they will apply for World Health Organization approval for one of the country’s homegrown covid-19 vaccines, as they announced that they had secured funding to produce 200 million vaccine doses for low income countries.

Full news article: [Covid-19: Cuba will request WHO approval for homegrown vaccine | The BMJ](https://www.bmj.com/content/376/bmj.o230)

**Title:** Covid-19: One in 23 people in England had infection in early January

Coronavirus infections in England were at their highest ever rate in early January this year, with an estimated one in 23 people infected, the ongoing REACT-1 monitoring study has reported.[**1**](https://www.bmj.com/content/376/bmj.o222#ref-1)

Findings from Imperial College London and Ipsos Mori covering 5-20 January show that the prevalence in England was 4.41%. This is more than three times the prevalence in the previous round of the survey in December, when one in 70 had the virus.

Infections reached a peak around 5 January before levelling off from mid-January, but they were still at extremely high levels. Schoolchildren have shown a rise in prevalence after returning to school this month.

Full news article: [Covid-19: One in 23 people in England had infection in early January | The BMJ](https://www.bmj.com/content/376/bmj.o222)

**Title:** Covid-19: CoronaVac immunity is strongest after boosting with a different vaccine

BMJ| 25th january

A booster dose of a covid-19 jab other than CoronaVac significantly increased antibodies in those who had received two doses of the Chinese vaccine, a study funded by Brazil's Ministry of Health has found.

A booster dose of Pfizer Biontech’s mRNA vaccine boosted antibody levels the most, followed by Oxford AstraZeneca, Janssen, and a third dose of CoronaVac. All booster vaccines were effective and safe, concluded the researchers at the University of Oxford, who co-led the study published in the *Lancet*.[**1**](https://www.bmj.com/content/376/bmj.o210#ref-1)

The findings will guide governments on how to boost their populations’ immunity in the face of the more infectious omicron variant.

Full news article: [Covid-19: CoronaVac immunity is strongest after boosting with a different vaccine | The BMJ](https://www.bmj.com/content/376/bmj.o210)

**Title:** Menstruation and covid-19 vaccination

BMJ| 26th january

Vaccination against covid-19 provides protection against the potentially serious consequences of SARS-CoV2 infection, but as the vaccines were rolled out into younger age groups, clinicians were increasingly approached by patients worried that the vaccine had caused a change to their periods.

More than 36 000 reports of menstrual changes or unexpected vaginal bleeding following covid-19 vaccination have so far been made to the yellow card surveillance scheme run by the UK Medicine and Healthcare Products Regulatory Agency (MHRA).[**1**](https://www.bmj.com/content/376/bmj.o142#ref-1) But as cycles vary naturally and the MHRA does not collect comparison data from unvaccinated people, these data cannot be used to establish whether menstrual changes increase after vaccination. A similar signal appeared in the US vaccine adverse event reporting system (VAERS), and as a result the National Institutes of Health allocated $1.67m (£1.2m; €1.4m) for research into a possible connection.[**2**](https://www.bmj.com/content/376/bmj.o142#ref-2)

The first of these studies has now reported.[**3**](https://www.bmj.com/content/376/bmj.o142#ref-3) The authors took advantage of an existing dataset from a menstrual cycle tracking app: 3959 Americans logged at least six consecutive cycles; 2403 of them were vaccinated and the remainder acted as a control group. In adjusted models, the first dose of vaccine had no effect on timing of the subsequent period, while the second dose was associated with a delay of 0.45 days (98.75% confidence interval 0.06 to 0.84).

Full article: [Menstruation and covid-19 vaccination | The BMJ](https://www.bmj.com/content/376/bmj.o142)

**Title:** Persistence of protection against SARS-CoV-2 clinical outcomes up to 9 months since vaccine completion: a retrospective observational analysis in Lombardy, Italy

the lancet – infectious diseases| 27th january

Background

Scarce information is available on the duration of the protective effect of COVID-19 vaccination against the risk of SARS-CoV-2 infection and its severe clinical consequences. We investigated the effect of time since vaccine completion on the SARS-CoV-2 infection and its severe forms.

Methods

In this retrospective observational analysis using the vaccination campaign integrated platform of the Italian region of Lombardy, 5 351 085 individuals aged 12 years or older who received complete vaccination from Jan 17 to July 31, 2021, were followed up from 14 days after vaccine completion until Oct 20, 2021. Changes over time in outcome rates (ie, SARS-CoV-2 infection and severe illness among vaccinated individuals) were analysed with age-period-cohort models. Trends in vaccine effectiveness (ie, outcomes comparison in vaccinated and unvaccinated individuals) were also measured.

Findings

Overall, 14 140 infections and 2450 severe illnesses were documented, corresponding to incidence rates of 6·7 (95% CI 6·6–6·8) and 1·2 (1·1–1·2) cases per 10 000 person-months, respectively. From the first to the ninth month since vaccine completion, rates increased from 4·6 to 10·2 infections, and from 1·0 to 1·7 severe illnesses every 10 000 person-months. These figures correspond to relative reduction of vaccine effectiveness of 54·9% (95% CI 48·3–60·6) for infection and of 40·0% (16·2–57·0) for severe illness. The increasing infection rate was greater for individuals aged 60 years or older who received adenovirus-vectored vaccines (from 4·0 to 23·5 cases every 10 000 person-months). The increasing severe illness rates were similar for individuals receiving mRNA-based vaccines (from 1·1 to 1·5 every 10 000 person-months) and adenovirus-vectored vaccines (from 0·5 to 0·9 every 10 000 person-months).

Interpretation

Although the risk of infection after vaccination, and even more of severe illness, remains low, the gradual increase in clinical outcomes related to SARS-CoV-2 infection suggests that the booster campaign should be accelerated and that social and individual protection measures against COVID-19 spread should not be abandoned.

Full article: [Persistence of protection against SARS-CoV-2 clinical outcomes up to 9 months since vaccine completion: a retrospective observational analysis in Lombardy, Italy - The Lancet Infectious Diseases](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00813-6/fulltext)

**Title:** Severe COVID-19 in pregnancy is almost exclusively limited to unvaccinated women – time for policies to change

THE LANCET – REGIONAL HEALTH EUROPE| 26th January

Pregnant women continue to be excluded from most clinical trials of COVID-19 vaccines and medication, despite very clear pre-pandemic guidance.1 There appears little incentive amongst regulators or pharmaceutical companies to change this. Compounded by their exclusion, there is considerable vaccine hesitancy amongst pregnant women.2 Such hesitancy persists, even though at present adverse outcomes of SARS-CoV-2 infection are increasing among pregnant and postpartum women in many countries,3 while these are improving in most other groups. The impact of the omicron variant is, as yet, unknown.

Full comment article: [Severe COVID-19 in pregnancy is almost exclusively limited to unvaccinated women – time for policies to change - The Lancet Regional Health – Europe](https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00006-0/fulltext)

**Title:** Safety and immunogenicity of an AS03-adjuvanted SARS-CoV-2 recombinant protein vaccine (CoV2 preS dTM) in healthy adults: interim findings from a phase 2, randomised, dose-finding, multicentre study

THE LANCET – INFECTIOUS DISEASES| 25th January

We evaluated our SARS-CoV-2 prefusion spike recombinant protein vaccine (CoV2 preS dTM) with different adjuvants, unadjuvanted, and in a one-injection and two-injection dosing schedule in a previous phase 1–2 study. Based on interim results from that study, we selected a two-injection schedule and the AS03 adjuvant for further clinical development. However, lower than expected antibody responses, particularly in older adults, and higher than expected reactogenicity after the second vaccination were observed. In the current study, we evaluated the safety and immunogenicity of an optimised formulation of CoV2 preS dTM adjuvanted with AS03 to inform progression to phase 3 clinical trial.

Full article: [Safety and immunogenicity of an AS03-adjuvanted SARS-CoV-2 recombinant protein vaccine (CoV2 preS dTM) in healthy adults: interim findings from a phase 2, randomised, dose-finding, multicentre study - The Lancet Infectious Diseases](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00764-7/fulltext)

**Title:** Intranasal COVID-19 vaccines: From bench to bed

eBIOMEDICINE| 24th January

Currently licensed COVID-19 vaccines are all designed for intramuscular (IM) immunization. However, vaccination today failed to prevent the virus infection through the upper respiratory tract, which is partially due to the absence of mucosal immunity activation. Despite the emerging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants, the next generation of COVID-19 vaccine is in demand and intranasal (IN) vaccination method has been demonstrated to be potent in inducing both mucosal and systemic immune responses. Presently, although not licensed, various IN vaccines against SARS-CoV-2 are under intensive investigation, with 12 candidates reaching clinical trials at different phases. In this review, we give a detailed description about current status of IN COVID-19 vaccines, including virus-vectored vaccines, recombinant subunit vaccines and live attenuated vaccines. The ongoing clinical trials for IN vaccines are highlighted. Additionally, the underlying mechanisms of mucosal immunity and potential mucosal adjuvants and nasal delivery devices are also summarized.

Full review: [Intranasal COVID-19 vaccines: From bench to bed - eBioMedicine (thelancet.com)](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00025-1/fulltext)

**Title:** SARS-CoV-2 infection and vaccine effectiveness in England (REACT-1): a series of cross-sectional random community surveys

THE Lancet respiratory medicine|24th january

Background

England has experienced a third wave of the COVID-19 epidemic since the end of May, 2021, coinciding with the rapid spread of the delta (B.1.617.2) variant, despite high levels of vaccination among adults. Vaccination rates (single dose) in England are lower among children aged 16–17 years and 12–15 years, whose vaccination in England commenced in August and September, 2021, respectively. We aimed to analyse the underlying dynamics driving patterns in SARS-CoV-2 prevalence during September, 2021, in England.

Methods

The REal-time Assessment of Community Transmission-1 (REACT-1) study, which commenced data collection in May, 2020, involves a series of random cross-sectional surveys in the general population of England aged 5 years and older. Using RT-PCR swab positivity data from 100 527 participants with valid throat and nose swabs in round 14 of REACT-1 (Sept 9–27, 2021), we estimated community-based prevalence of SARS-CoV-2 and vaccine effectiveness against infection by combining round 14 data with data from round 13 (June 24 to July 12, 2021; n=172 862).

Findings

During September, 2021, we estimated a mean RT-PCR positivity rate of 0·83% (95% CrI 0·76–0·89), with a reproduction number (R) overall of 1·03 (95% CrI 0·94–1·14). Among the 475 (62·2%) of 764 sequenced positive swabs, all were of the delta variant; 22 (4·63%; 95% CI 3·07–6·91) included the Tyr145His mutation in the spike protein associated with the AY.4 sublineage, and there was one Glu484Lys mutation. Age, region, key worker status, and household size jointly contributed to the risk of swab positivity. The highest weighted prevalence was observed among children aged 5–12 years, at 2·32% (95% CrI 1·96–2·73) and those aged 13–17 years, at 2·55% (2·11–3·08). The SARS-CoV-2 epidemic grew in those aged 5–11 years, with an R of 1·42 (95% CrI 1·18–1·68), but declined in those aged 18–54 years, with an R of 0·81 (0·68–0·97). At ages 18–64 years, the adjusted vaccine effectiveness against infection was 62·8% (95% CI 49·3–72·7) after two doses compared to unvaccinated people, for all vaccines combined, 44·8% (22·5–60·7) for the ChAdOx1 nCov-19 (Oxford–AstraZeneca) vaccine, and 71·3% (56·6–81·0) for the BNT162b2 (Pfizer–BioNTech) vaccine. In individuals aged 18 years and older, the weighted prevalence of swab positivity was 0·35% (95% CrI 0·31–0·40) if the second dose was administered up to 3 months before their swab but 0·55% (0·50–0·61) for those who received their second dose 3–6 months before their swab, compared to 1·76% (1·60–1·95) among unvaccinated individuals.

Interpretation

In September, 2021, at the start of the autumn school term in England, infections were increasing exponentially in children aged 5–17 years, at a time when vaccination rates were low in this age group. In adults, compared to those who received their second dose less than 3 months ago, the higher prevalence of swab positivity at 3–6 months following two doses of the COVID-19 vaccine suggests an increased risk of breakthrough infections during this period. The vaccination programme needs to reach children as well as unvaccinated and partially vaccinated adults to reduce SARS-CoV-2 transmission and associated disruptions to work and education.

Full article: [SARS-CoV-2 infection and vaccine effectiveness in England (REACT-1): a series of cross-sectional random community surveys - The Lancet Respiratory Medicine](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00542-7/fulltext)

**Title:** Safety and immunogenicity of the SARS-CoV-2 ARCoV mRNA vaccine in Chinese adults: a randomised, double-blind, placebo-controlled, phase 1 trial

the lancet – microbe| 24th january

Background

Safe and effective vaccines are urgently needed to end the COVID-19 pandemic caused by SARS-CoV-2 infection. We aimed to assess the preliminary safety, tolerability, and immunogenicity of an mRNA vaccine ARCoV, which encodes the SARS-CoV-2 spike protein receptor-binding domain (RBD).

Methods

This single centre, double-blind, randomised, placebo-controlled, dose-escalation, phase 1 trial of ARCoV was conducted at Shulan (Hangzhou) hospital in Hangzhou, Zhejiang province, China. Healthy adults aged 18–59 years negative for SARS-CoV-2 infection were enrolled and randomly assigned using block randomisation to receive an intramuscular injection of vaccine or placebo. Vaccine doses were 5 μg, 10 μg, 15 μg, 20 μg, and 25 μg. The first six participants in each block were sentinels and along with the remaining 18 participants, were randomly assigned to groups (5:1). In block 1 sentinels were given the lowest vaccine dose and after a 4-day observation with confirmed safety analyses, the remaining 18 participants in the same dose group proceeded and sentinels in block 2 were given their first administration on a two-dose schedule, 28 days apart. All participants, investigators, and staff doing laboratory analyses were masked to treatment allocation. Humoral responses were assessed by measuring anti-SARS-CoV-2 RBD IgG using a standardised ELISA and neutralising antibodies using pseudovirus-based and live SARS-CoV-2 neutralisation assays. SARS-CoV-2 RBD-specific T-cell responses, including IFN-γ and IL-2 production, were assessed using an enzyme-linked immunospot (ELISpot) assay. The primary outcome for safety was incidence of adverse events or adverse reactions within 60 min, and at days 7, 14, and 28 after each vaccine dose. The secondary safety outcome was abnormal changes detected by laboratory tests at days 1, 4, 7, and 28 after each vaccine dose. For immunogenicity, the secondary outcome was humoral immune responses: titres of neutralising antibodies to live SARS-CoV-2, neutralising antibodies to pseudovirus, and RBD-specific IgG at baseline and 28 days after first vaccination and at days 7, 15, and 28 after second vaccination. The exploratory outcome was SARS-CoV-2-specific T-cell responses at 7 days after the first vaccination and at days 7 and 15 after the second vaccination. This trial is registered with [www.chictr.org.cn](http://www.chictr.org.cn/) (ChiCTR2000039212).

Findings

Between Oct 30 and Dec 2, 2020, 230 individuals were screened and 120 eligible participants were randomly assigned to receive five-dose levels of ARCoV or a placebo (20 per group). All participants received the first vaccination and 118 received the second dose. No serious adverse events were reported within 56 days after vaccination and the majority of adverse events were mild or moderate. Fever was the most common systemic adverse reaction (one [5%] of 20 in the 5 μg group, 13 [65%] of 20 in the 10 μg group, 17 [85%] of 20 in the 15 μg group, 19 [95%] of 20 in the 20 μg group, 16 [100%] of 16 in the 25 μg group; p<0·0001). The incidence of grade 3 systemic adverse events were none (0%) of 20 in the 5 μg group, three (15%) of 20 in the 10 μg group, six (30%) of 20 in the 15 μg group, seven (35%) of 20 in the 20 μg group, five (31%) of 16 in the 25 μg group, and none (0%) of 20 in the placebo group (p=0·0013). As expected, the majority of fever resolved in the first 2 days after vaccination for all groups. The incidence of solicited systemic adverse events was similar after administration of ARCoV as a first or second vaccination. Humoral immune responses including anti-RBD IgG and neutralising antibodies increased significantly 7 days after the second dose and peaked between 14 and 28 days thereafter. Specific T-cell response peaked between 7 and 14 days after full vaccination. 15 μg induced the highest titre of neutralising antibodies, which was about twofold more than the antibody titre of convalescent patients with COVID-19.

Interpretation

ARCoV was safe and well tolerated at all five doses. The acceptable safety profile, together with the induction of strong humoral and cellular immune responses, support further clinical testing of ARCoV at a large scale.

Full article: [Safety and immunogenicity of the SARS-CoV-2 ARCoV mRNA vaccine in Chinese adults: a randomised, double-blind, placebo-controlled, phase 1 trial - The Lancet Microbe](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00280-9/fulltext)

**Title:** Homologous and Heterologous Covid-19 Booster Vaccinations

NEJM| 26th JANUARY

**BACKGROUND**

Although the three vaccines against coronavirus disease 2019 (Covid-19) that have received emergency use authorization in the United States are highly effective, breakthrough infections are occurring. Data are needed on the serial use of homologous boosters (same as the primary vaccine) and heterologous boosters (different from the primary vaccine) in fully vaccinated recipients.

**METHODS**

In this phase 1–2, open-label clinical trial conducted at 10 sites in the United States, adults who had completed a Covid-19 vaccine regimen at least 12 weeks earlier and had no reported history of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection received a booster injection with one of three vaccines: mRNA-1273 (Moderna) at a dose of 100 μg, Ad26.COV2.S (Johnson & Johnson–Janssen) at a dose of 5×1010 virus particles, or BNT162b2 (Pfizer–BioNTech) at a dose of 30 μg. The primary end points were safety, reactogenicity, and humoral immunogenicity on trial days 15 and 29.

**RESULTS**

Of the 458 participants who were enrolled in the trial, 154 received mRNA-1273, 150 received Ad26.COV2.S, and 153 received BNT162b2 as booster vaccines; 1 participant did not receive the assigned vaccine. Reactogenicity was similar to that reported for the primary series. More than half the recipients reported having injection-site pain, malaise, headache, or myalgia. For all combinations, antibody neutralizing titers against a SARS-CoV-2 D614G pseudovirus increased by a factor of 4 to 73, and binding titers increased by a factor of 5 to 55. Homologous boosters increased neutralizing antibody titers by a factor of 4 to 20, whereas heterologous boosters increased titers by a factor of 6 to 73. Spike-specific T-cell responses increased in all but the homologous Ad26.COV2.S-boosted subgroup. CD8+ T-cell levels were more durable in the Ad26.COV2.S-primed recipients, and heterologous boosting with the Ad26.COV2.S vaccine substantially increased spike-specific CD8+ T cells in the mRNA vaccine recipients.

**CONCLUSIONS**

Homologous and heterologous booster vaccines had an acceptable safety profile and were immunogenic in adults who had completed a primary Covid-19 vaccine regimen at least 12 weeks earlier. (Funded by the National Institute of Allergy and Infectious Diseases; DMID 21-0012 ClinicalTrials.gov number, [**NCT04889209. opens in new tab**](http://clinicaltrials.gov/show/NCT04889209).)

Full article: [Homologous and Heterologous Covid-19 Booster Vaccinations | NEJM](https://www.nejm.org/doi/full/10.1056/NEJMoa2116414?query=featured_coronavirus)

**Title:** Assessment of a Smartphone-Based Loop-Mediated Isothermal Amplification Assay for Detection of SARS-CoV-2 and Influenza Viruses

jama network open| 28th january

**Question**  Can loop-mediated isothermal amplification (LAMP)-based methodology coupled with smartphone detection provide an inexpensive, rapid, sensitive, and reliable platform for COVID-19 and influenza testing?

**Findings**  In this cohort study of saliva samples from 50 community-based patients, the smartphone-based LAMP assay detected SARS-CoV-2 infection and exhibited concordance with reverse transcriptase–quantitative polymerase chain reaction tests.

**Meaning**  These findings suggest that the smartphone-based LAMP assay offers an additional tool to detect COVID-19 that can be readily modified in response to novel SARS-CoV-2 variants and other pathogens with pandemic potential including influenza.

Full article: [Assessment of a Smartphone-Based Loop-Mediated Isothermal Amplification Assay for Detection of SARS-CoV-2 and Influenza Viruses | Infectious Diseases | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788464)

**Title:** Myocarditis Cases Reported After mRNA-Based COVID-19 Vaccination in the US From December 2020 to August 2021

Jama| 25th january

**Question**  What is the risk of myocarditis after mRNA-based COVID-19 vaccination in the US?

**Findings**  In this descriptive study of 1626 cases of myocarditis in a national passive reporting system, the crude reporting rates within 7 days after vaccination exceeded the expected rates across multiple age and sex strata. The rates of myocarditis cases were highest after the second vaccination dose in adolescent males aged 12 to 15 years (70.7 per million doses of the BNT162b2 vaccine), in adolescent males aged 16 to 17 years (105.9 per million doses of the BNT162b2 vaccine), and in young men aged 18 to 24 years (52.4 and 56.3 per million doses of the BNT162b2 vaccine and the mRNA-1273 vaccine, respectively).

**Meaning**  Based on passive surveillance reporting in the US, the risk of myocarditis after receiving mRNA-based COVID-19 vaccines was increased across multiple age and sex strata and was highest after the second vaccination dose in adolescent males and young men.

Full article: [Myocarditis Cases Reported After mRNA-Based COVID-19 Vaccination in the US From December 2020 to August 2021 | Cardiology | JAMA | JAMA Network](https://jamanetwork.com/journals/jama/fullarticle/2788346)

Health management

**Title:** Covid-19: Long term plan on living with pandemic to come in spring, says Javid

BMJ| 27th january

The government is to set out a plan for how the UK can manage covid-19 in the long term and to prepare for any future pandemics.

Expected by this spring, the plan will be a cross department collaboration, bringing together all the learning from the current pandemic and an assessment of the most effective strategies for tackling SARS-CoV-2.

Full news article: [Covid-19: Long term plan on living with pandemic to come in spring, says Javid | The BMJ](https://www.bmj.com/content/376/bmj.o235)

**Title:** The Covid-19 Vaccination Programme: Trials, Tribulations And Successes

the kings fund| 31st january

The Covid-19 vaccination programme has been one of the key successes of the UK's response to the pandemic. Based on interviews with a wide range of people involved in the programme, this report sets out what the roll-out in England has achieved.

* [Report](https://www.kingsfund.org.uk/sites/default/files/2022-01/The%20Covid-19%20Vaccination%20Programme%20online%20version_2%20%281%29.pdf)
* [More detail](https://www.kingsfund.org.uk/publications/covid-19-vaccination-programme)

other

**Title:** Covid-19: unravelling the conundrum of omicron and deaths

bmj| 28th january

Covid deaths in the UK are at their highest since February 2021 despite omicron being less severe than previous variants. **Gareth Iacobucci** investigates why

Confidence is growing among experts and ministers in the UK that omicron is milder than previous variants of SARS-CoV-2, and politicians and scientists alike are increasingly bullish that the worst of the covid-19 pandemic is behind us.[**1**](https://www.bmj.com/content/376/bmj.o254#ref-1)[**2**](https://www.bmj.com/content/376/bmj.o254#ref-2) At the same time, the number of people dying from covid in the UK is higher than it has been since February 2021.

Full news article: [Covid-19: unravelling the conundrum of omicron and deaths | The BMJ](https://www.bmj.com/content/376/bmj.o254)

**Title:** Covid-19: Lower vaccination rates partly explain higher death rates among minority ethnic groups

BMJ| 27th january

Death rates from covid-19 remain higher for most minority ethnic groups compared with people identifying as white British, and some of that disparity is because of their lower uptake of vaccinations, show data from the Office for National Statistics (ONS).[**1**](https://www.bmj.com/content/376/bmj.o233#ref-1)

Throughout the pandemic covid-19 mortality has been higher in most minority ethnic groups compared with white British people.

Vahé Nafilyan, senior statistician at the ONS, said, “As already highlighted in our analyses of earlier periods, these differences in mortality are largely explained by sociodemographic and economic factors and health. For the first time, we show that the lower vaccination coverage in some ethnic groups also contributes to the elevated risk of covid-19 death, particularly in the black African and black Caribbean groups.”

Full news article: [Covid-19: Lower vaccination rates partly explain higher death rates among minority ethnic groups | The BMJ](https://www.bmj.com/content/376/bmj.o233)

**Title:** Association of Child Masking With COVID-19–Related Closures in US Childcare Programs

JAMA Network open| 27th January

**Question**  Is child masking associated with reduced COVID-19–related childcare program closures?

**Findings**  In this survey study of 6654 childcare professionals from all 50 states, child masking at baseline (May 22 to June 8, 2020) was associated with a 13% reduction in program closure within the following year, and continued child masking throughout the 1-year study period was associated with a 14% reduction in program closure.

**Meaning**  These results suggest that masking of children in childcare programs is associated with reduced program closures, supporting current masking recommendation in younger children provided by the Centers for Disease Control and Prevention.

Full article: [Association of Child Masking With COVID-19–Related Closures in US Childcare Programs | Pediatrics | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788457)

**Title:** Two Monthly Report On The Status On The Non-Devolved Provisions Of The Coronavirus Act 2020: January 2022

**Department of Health and Social Care| 28th January**  
The Coronavirus Act 2020 gives the government powers to take the right action to respond effectively to the progress of the coronavirus (Covid-19) pandemic. These powers are temporary and designed to be switched on when necessary, and off when no longer needed. The act requires ministers to report every two months on which powers are currently active.

* [Report](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1050693/coronavirus-act-2020-eleventh-two-monthly-report-web-accessible.pdf)
* [Department of Health and Social Care - publications](https://www.gov.uk/government/publications/coronavirus-act-report-january-2022)

We

[TRFT Library & Knowledge Service](https://www.trftlibraryknowledge.com/) aim to bring together the latest guidelines, research and news on Covid-19 through our [Covid-19 portal](https://www.trftlibraryknowledge.com/coronavirus.html). For daily updates on Covid-19 visit our '[Latest Health](https://trfthealthweeklydigest.wordpress.com/)' newsfeed, or use the hashtag [#covid19rftlks](https://twitter.com/hashtag/covid19rftlks?src=hashtag_click) to see our latest tweets on Covid-19 research, guidelines and news.

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