COVID-19 weekly update

14th March 2022

**clinical management**

**Title:** Coronavirus disease 2019 (COVID-19) [evidence-based summary]

bmj best practice| 14th march 2022

Updates: 1) WHO recommends Sotrovimab and Baricitinib to treat COVID-19. 2) NICE recommends monoclonal antibodies for people not in hospital. 3) FDA revises authorisations for monoclonal antibodies in the US. 4) First protein subunit vaccine approved in the UK - Novavax’s vaccine, Nuvaxovid®, has been approved.]
*Available with an NHS OpenAthens password*[https://bestpractice.bmj.com/topics/en-gb/3000201](http://comm.knowledgeshare.nhs.uk/ls/click?upn=w6kEKPngG5Unp9AJ7fP-2BOfbEgYndYm2221mENDJVnP7wNlr-2Bb8pWgafGYb24aVDn8v2sjyts0qp7ITMAWz8Ukw-3D-3DVzJZ_RL1JExwc8cKmCy5bELgKVa8D9r4HITdF-2BpCEXyu5SoWRBLfnRpm2WCJTckV0IEILWgWmKPyaK30XbdKdLowzQxp74iBtcCYQ637fc99r-2BWgGRuVe-2BTNzGLnkroRjROA2q8tg1yoWI-2B7AgiVQynOPGnoGh8J8KiSWFlIOEEpAdD0VK-2FOsGDV2tvZ0CuO1CZYpZprlrgFeFEatu2lQRrf569-2FllFDMWMWSe4ArbZqUOLrSf-2FCFyyDUH1vDe-2B8bBkdQSa34iL1qRqnkqh16lYYChElAWrozQUuhG5e9wkSdIfNyH1DUb4QbUCpEafLRit42skF3ewJRSofZaU4UEqFK7LUaVBoYfSJXdDK5P9FbWPtNX-2FySkncH1QYxHPpaOhS8)

**Title:** Efficacy and safety of CD24Fc in hospitalised patients with COVID-19: a randomised, double-blind, placebo-controlled, phase 3 study

the lancet infectious diseases| 11th march 2022

Non-antiviral therapeutic options are required for the treatment of hospitalised patients with COVID-19. CD24Fc is an immunomodulator with potential to reduce the exaggerated inflammatory response to tissue injuries. We aimed to evaluate the safety and efficacy of CD24Fc in hospitalised adults with COVID-19 receiving oxygen support. Methods: We conducted a randomised, double-blind, placebo-controlled, phase 3 study at nine medical centres in the USA. Hospitalised patients (age ≥18 years) with confirmed SARS-CoV-2 infection who were receiving oxygen support and standard of care were randomly assigned (1:1) by site-stratified block randomisation to receive a single intravenous infusion of CD24Fc 480 mg or placebo. The study funder, investigators, and patients were masked to treatment group assignment. The primary endpoint was time to clinical improvement over 28 days, defined as time that elapsed between a baseline National Institute of Allergy and Infectious Diseases ordinal scale score of 2–4 and reaching a score of 5 or higher or hospital discharge. The prespecified primary interim analysis was done when 146 participants reached the time to clinical improvement endpoint. Efficacy was assessed in the intention-to-treat population. Safety was assessed in the as-treated population. This study is registered with ClinicalTrials.gov, NCT04317040.

Findings: Between April 24 and Sept 22, 2020, 243 hospitalised patients were assessed for eligibility and 234 were enrolled and randomly assigned to receive CD24Fc (n=116) or placebo (n=118). The prespecified interim analysis was done when 146 participants reached the time to clinical improvement endpoint among 197 randomised participants. In the interim analysis, the 28-day clinical improvement rate was 82% (81 of 99) for CD24Fc versus 66% (65 of 98) for placebo; median time to clinical improvement was 6·0 days (95% CI 5·0–8·0) in the CD24Fc group versus 10·0 days (7·0–15·0) in the placebo group (hazard ratio [HR] 1·61, 95% CI 1·16–2·23; log-rank p=0·0028, which crossed the prespecified efficacy boundary [α=0·0147]). 37 participants were randomly assigned after the interim analysis data cutoff date; among the 234 randomised participants, median time to clinical improvement was 6·0 days (95% CI 5·0–9·0) in the CD24Fc group versus 10·5 days (7·0–15·0) in the placebo group (HR 1·40, 95% CI 1·02–1·92; log-rank p=0·037). The proportion of participants with disease progression within 28 days was 19% (22 of 116) in the CD24Fc group versus 31% (36 of 118) in the placebo group (HR 0·56, 95% CI 0·33–0·95; unadjusted p=0·031). The incidences of adverse events and serious adverse events were similar in both groups. No treatment-related adverse events were observed.

Interpretation: CD24Fc is generally well tolerated and accelerates clinical improvement of hospitalised patients with COVID-19 who are receiving oxygen support. These data suggest that targeting inflammation in response to tissue injuries might provide a therapeutic option for patients hospitalised with COVID-19.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00058-5/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900058-5/fulltext)

**title:** CD24Fc: an emerging COVID-19 therapy [comment]

the lancet infectious diseases | 11th march 2022

…The study was well designed, with near-complete protocol adherence and minimal loss to follow-up. However, the trial enrolled participants between April and September, 2020, and preceded landmark clinical trials of dexamethasone,3 remdesivir,4 and interleukin-6 (IL-6) receptor antagonists in the treatment of severe COVID-19. As a result, CD24Fc infusion was compared with an outdated standard of care that included a combination of experimental corticosteroids, remdesivir, and convalescent plasma given at the discretion of the treating physician. Since the enrolment period ended, trials have shown that convalescent plasma was not associated with reduced time to clinical improvement and IL-6 receptor antagonists have emerged as an important part of the COVID-19 treatment framework….
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00125-6/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900125-6/fulltext)

**Title:** Association Between Dexamethasone Treatment After Hospital Discharge for Patients With COVID-19 Infection and Rates of Hospital Readmission and Mortality

JAMA| 8th march 2022

Question Is continuing use of dexamethasone, 6 mg/d, at discharge for patients with COVID-19 who received less than 10 days of dexamethasone treatment during hospitalization associated with readmission or mortality after discharge?

Findings In a cohort of 1164 patients with COVID-19 who received less than 10 days of dexamethasone, 6 mg/d, during hospitalization, the rate of readmission or mortality within 14 days of discharge was 9.1% among patients who continued dexamethasone treatment compared with 11.4% among patients who did not. The difference was not statistically significant.

Meaning The findings of this study suggest that prescribing dexamethasone at discharge for patients hospitalized with COVID-19 who received less than 10 days of dexamethasone is not associated with a reduction in readmission or mortality.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2789710>

**title:** Once Viewed as a Promising COVID-19 Treatment, Convalescent Plasma Falls Out of Favor

jama| 9th march 2022

In the pandemic’s initial dark days, physicians and patients and their families were desperate for effective COVID-19 treatments. They didn’t yet have monoclonal antibodies or antiviral pills to lessen the ravages of the disease, so many turned to a therapy more than a century old. At the very least, they figured, convalescent plasma, donated by people who’d recovered from COVID-19, couldn’t hurt, and the SARS-CoV-2 antibodies it was presumed to contain could enhance patients’ defenses against COVID-19. “There was a preconceived notion of efficacy,” H. Clifford Lane, MD, deputy director for clinical research and special projects at the National Institute of Allergy and Infectious Diseases, said in a recent interview.

Three reports from Wuhan, China, published in 2020 in JAMA, the Proceedings of the National Academy of Sciences, and the Journal of Medical Virology, showed that patients’ viral load decreased and their symptoms improved following infusions of convalescent plasma. But the studies involved only a total of 21 patients; the authors of all 3 articles noted that clinical trials were needed to confirm the findings.

 Nevertheless, while trials were being planned, US hospitals began infusing patients with COVID-19 with convalescent plasma through the US Food and Drug Administration’s (FDA’s) Expanded Access Program (EAP). Approximately 94 000 people hospitalized with COVID-19 in the US had received convalescent plasma infusions by August 2020, when the FDA ended the EAP and authorized the golden liquid for emergency use.

 A December 2021 analysis of EAP data in PLOS Medicine demonstrated convalescent plasma’s safety in patients hospitalized with COVID-19—the incidence of serious adverse events was less than 1%. But because the study didn’t include a control or comparator group, “the data should not be used to infer definitive treatment effects,” the authors noted.

As other COVID-19 treatments became available, convalescent plasma’s early promise didn’t pan out in randomized clinical trials. “I don’t think convalescent plasma is a first-line therapy at this point,” Kevin Schulman, MD, a professor of medicine at the Stanford University School of Medicine who has studied the treatment, said in an interview.
<https://jamanetwork.com/journals/jama/fullarticle/2790074>

**title:** US Maternal Mortality Rate Rose Sharply During COVID-19 Pandemic’s First Year

jama| 8th march 2022

The rate of maternal mortality, already increasing in recent years, surged in 2020, particularly among Black and Hispanic women, according to a new report from the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention.

In 2020, there were 861 total maternal deaths, compared with 754 in 2019 and 658 in 2018. That translated to 23.8 deaths per 100 000 live births in 2020, up from 20.1 deaths per 100 000 live births in 2019.
<https://jamanetwork.com/journals/jama-health-forum/fullarticle/2790036>

**title:** Real-world evaluation of rapid and laboratory-free COVID-19 triage for emergency care: external validation and pilot deployment of artificial intelligence driven screening

THE LANCET digitial health| 9th march 2022

Background

Uncertainty in patients' COVID-19 status contributes to treatment delays, nosocomial transmission, and operational pressures in hospitals. However, the typical turnaround time for laboratory PCR remains 12–24 h and lateral flow devices (LFDs) have limited sensitivity. Previously, we have shown that artificial intelligence-driven triage (CURIAL-1.0) can provide rapid COVID-19 screening using clinical data routinely available within 1 h of arrival to hospital. Here, we aimed to improve the time from arrival to the emergency department to the availability of a result, do external and prospective validation, and deploy a novel laboratory-free screening tool in a UK emergency department.

Methods: We optimised our previous model, removing less informative predictors to improve generalisability and speed, developing the CURIAL-Lab model with vital signs and readily available blood tests (full blood count [FBC]; urea, creatinine, and electrolytes; liver function tests; and C-reactive protein) and the CURIAL-Rapide model with vital signs and FBC alone. Models were validated externally for emergency admissions to University Hospitals Birmingham, Bedfordshire Hospitals, and Portsmouth Hospitals University National Health Service (NHS) trusts, and prospectively at Oxford University Hospitals, by comparison with PCR testing. Next, we compared model performance directly against LFDs and evaluated a combined pathway that triaged patients who had either a positive CURIAL model result or a positive LFD to a COVID-19-suspected clinical area. Lastly, we deployed CURIAL-Rapide alongside an approved point-of-care FBC analyser to provide laboratory-free COVID-19 screening at the John Radcliffe Hospital (Oxford, UK). Our primary improvement outcome was time-to-result, and our performance measures were sensitivity, specificity, positive and negative predictive values, and area under receiver operating characteristic curve (AUROC).

Findings: 72 223 patients met eligibility criteria across the four validating hospital groups, in a total validation period spanning Dec 1, 2019, to March 31, 2021. CURIAL-Lab and CURIAL-Rapide performed consistently across trusts (AUROC range 0·858–0·881, 95% CI 0·838–0·912, for CURIAL-Lab and 0·836–0·854, 0·814–0·889, for CURIAL-Rapide), achieving highest sensitivity at Portsmouth Hospitals (84·1%, Wilson's 95% CI 82·5–85·7, for CURIAL-Lab and 83·5%, 81·8–85·1, for CURIAL-Rapide) at specificities of 71·3% (70·9–71·8) for CURIAL-Lab and 63·6% (63·1–64·1) for CURIAL-Rapide. When combined with LFDs, model predictions improved triage sensitivity from 56·9% (51·7–62·0) for LFDs alone to 85·6% with CURIAL-Lab (81·6–88·9; AUROC 0·925) and 88·2% with CURIAL-Rapide (84·4–91·1; AUROC 0·919), thereby reducing missed COVID-19 cases by 65% with CURIAL-Lab and 72% with CURIAL-Rapide. For the prospective deployment of CURIAL-Rapide, 520 patients were enrolled for point-of-care FBC analysis between Feb 18 and May 10, 2021, of whom 436 received confirmatory PCR testing and ten (2·3%) tested positive. Median time from arrival to a CURIAL-Rapide result was 45 min (IQR 32–64), 16 min (26·3%) sooner than with LFDs (61 min, 37–99; log-rank p<0·0001), and 6 h 52 min (90·2%) sooner than with PCR (7 h 37 min, 6 h 5 min to 15 h 39 min; p<0·0001). Classification performance was high, with sensitivity of 87·5% (95% CI 52·9–97·8), specificity of 85·4% (81·3–88·7), and negative predictive value of 99·7% (98·2–99·9). CURIAL-Rapide correctly excluded infection for 31 (58·5%) of 53 patients who were triaged by a physician to a COVID-19-suspected area but went on to test negative by PCR.

Interpretation: Our findings show the generalisability, performance, and real-world operational benefits of artificial intelligence-driven screening for COVID-19 over standard-of-care in emergency departments. CURIAL-Rapide provided rapid, laboratory-free screening when used with near-patient FBC analysis, and was able to reduce the number of patients who tested negative for COVID-19 but were triaged to COVID-19-suspected areas.
[https://www.thelancet.com/journals/landig/article/PIIS2589-7500(21)00272-7/fulltext](https://www.thelancet.com/journals/landig/article/PIIS2589-7500%2821%2900272-7/fulltext)

**title:** Triage in the time of COVID-19 [comment]

THE LANCEt digital health| 9th march 2022

…Considering the study presented by Soltan and colleagues, the key message is simple: the time has come for more effective, rapid, and available screening and triage tools. CURIAL devices represent an elegant breakthrough to enhance the clinical decision-making process in the age of artificial intelligence. As we are now facing the COVID-19 fourth wave, we are confident that artificial intelligence-driven triage will meet the challenge of optimising the early detection of patients with COVID-19 infection, reducing the spread of COVID-19 in emergency departments and in-hospital contamination.
[https://www.thelancet.com/journals/landig/article/PIIS2589-7500(22)00001-2/fulltext](https://www.thelancet.com/journals/landig/article/PIIS2589-7500%2822%2900001-2/fulltext)

**title:** Efficacy of Antiviral Agents against the SARS-CoV-2 Omicron Subvariant BA.2

new england journal of medicine| 9th march 2022

The omicron (B.1.1.529) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is responsible for coronavirus disease 2019 (Covid-19), has spread rapidly around the world and has already become the predominant variant circulating in many countries. As of February 2022, omicron variants have been divided into four distinct sublineages: BA.1, BA.1.1, BA.2, and BA.3.1 Most circulating omicron variants belong to sublineage BA.1; however, in Denmark, India, and the Philippines, the sublineage BA.2 is now becoming dominant.

As compared with the Wuhan/Hu-1/2019 reference strain, the sublineage BA.2 of the omicron variant has 16 amino acid substitutions in the receptor-binding domain of the spike (S) protein of SARS-CoV-2,2 which is the primary target for monoclonal antibody–based therapy. The BA.2 and BA.1 variants share 12 of these 16 substitutions; however, BA.2 has four substitutions in the receptor-binding domain (i.e., S371F, T376A, D405N, and R408S) that differ from those in BA.1. These findings suggest that there may be differences in the effectiveness of monoclonal antibodies against these different omicron sublineages.

Accordingly, we examined the neutralizing ability of therapeutic monoclonal antibodies that have been approved by the Food and Drug Administration, individually and in combination, against the omicron BA.2 subvariant hCoV-19/Japan/UT-NCD1288-2N/2022 (omicron/BA.2; NCD1288), which was isolated from a traveler who arrived in Japan from India….

…The susceptibilities of omicron/BA.2 (NCD1288) to remdesivir, molnupiravir, and nirmatrelvir were similar to those of the ancestral strain and other variants of concern (i.e., 50% inhibitory concentration values for these three agents that differed by factors of 2.5 to 4.5, 0.7 to 1.6, and 1.5 to 3.3, respectively) (**Table 1**).[**3**](https://www.nejm.org/doi/full/10.1056/NEJMc2201933?query=featured_coronavirus) Clinical studies are warranted to determine whether these antiviral therapies are indeed effective against omicron/BA.2 infections. Our data indicate that some therapeutic monoclonal antibodies (REGN10987–REGN10933, COV2-2196–COV2-2130, and S309) have lower neutralizing activity against omicron/BA.2 than against earlier variant strains.
<https://www.nejm.org/doi/full/10.1056/NEJMc2201933?query=featured_coronavirus>

**title:** Resistance Mutations in SARS-CoV-2 Delta Variant after Sotrovimab Use

THE LANCEt digital health| 9th march 2022

Sotrovimab is a monoclonal antibody that is available under emergency use authorization for the treatment of patients who are at risk for progression of coronavirus disease 2019 (Covid-19) to severe disease.1 Sotrovimab is thought to neutralize all sarbecoviruses, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), by binding to a highly conserved epitope within the receptor-binding domain.2 However, the use of SARS-CoV-2–specific monoclonal antibodies to target a single viral epitope warrants caution because of the risk of rapid development of mutations that confer resistance after exposure to these antibodies.2-4 Mutations at positions S:E340K/A/V and S:P337L/T (Figure 1A) have been associated with a reduction by a factor of 100 to 297 in neutralization by sotrovimab.5

We reviewed the first 100 consecutive patients who received sotrovimab at health care facilities in the Western Sydney Local Health District in New South Wales, Australia, during the B.1.617.2 (delta) variant outbreak between August and November 2021 …

…These data show the persistence of viable SARS-CoV-2 in patients after sotrovimab infusions and the rapid development of spike gene mutations associated with high-level sotrovimab resistance in vitro. These findings underscore the importance of stewardship of monoclonal antibodies, particularly because sotrovimab is one of the few monoclonal antibodies with retained activity against the B.1.1.529 (omicron) variant.1 Postmarketing genomic surveillance of patients who receive monoclonal antibodies for the treatment of SARS-CoV-2 infection is prudent in order to minimize the risk of both treatment failure and the transmission of potentially resistant SARS-CoV-2 variants in health care settings and the community, given that SARS-CoV-2 may be isolated up to 24 days after sotrovimab treatment.
<https://www.nejm.org/doi/full/10.1056/NEJMc2120219?query=featured_coronavirus>

**covid rates:**

**title:** Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21

The Lancet| 10th mARCH 2022

Background: Mortality statistics are fundamental to public health decision making. Mortality varies by time and location, and its measurement is affected by well known biases that have been exacerbated during the COVID-19 pandemic. This paper aims to estimate excess mortality from the COVID-19 pandemic in 191 countries and territories, and 252 subnational units for selected countries, from Jan 1, 2020, to Dec 31, 2021. Methods: All-cause mortality reports were collected for 74 countries and territories and 266 subnational locations (including 31 locations in low-income and middle-income countries) that had reported either weekly or monthly deaths from all causes during the pandemic in 2020 and 2021, and for up to 11 year previously. In addition, we obtained excess mortality data for 12 states in India. Excess mortality over time was calculated as observed mortality, after excluding data from periods affected by late registration and anomalies such as heat waves, minus expected mortality. Six models were used to estimate expected mortality; final estimates of expected mortality were based on an ensemble of these models. Ensemble weights were based on root mean squared errors derived from an out-of-sample predictive validity test. As mortality records are incomplete worldwide, we built a statistical model that predicted the excess mortality rate for locations and periods where all-cause mortality data were not available. We used least absolute shrinkage and selection operator (LASSO) regression as a variable selection mechanism and selected 15 covariates, including both covariates pertaining to the COVID-19 pandemic, such as seroprevalence, and to background population health metrics, such as the Healthcare Access and Quality Index, with direction of effects on excess mortality concordant with a meta-analysis by the US Centers for Disease Control and Prevention. With the selected best model, we ran a prediction process using 100 draws for each covariate and 100 draws of estimated coefficients and residuals, estimated from the regressions run at the draw level using draw-level input data on both excess mortality and covariates. Mean values and 95% uncertainty intervals were then generated at national, regional, and global levels. Out-of-sample predictive validity testing was done on the basis of our final model specification.

Findings: Although reported COVID-19 deaths between Jan 1, 2020, and Dec 31, 2021, totalled 5·94 million worldwide, we estimate that 18·2 million (95% uncertainty interval 17·1–19·6) people died worldwide because of the COVID-19 pandemic (as measured by excess mortality) over that period. The global all-age rate of excess mortality due to the COVID-19 pandemic was 120·3 deaths (113·1–129·3) per 100 000 of the population, and excess mortality rate exceeded 300 deaths per 100 000 of the population in 21 countries. The number of excess deaths due to COVID-19 was largest in the regions of south Asia, north Africa and the Middle East, and eastern Europe. At the country level, the highest numbers of cumulative excess deaths due to COVID-19 were estimated in India (4·07 million [3·71–4·36]), the USA (1·13 million [1·08–1·18]), Russia (1·07 million [1·06–1·08]), Mexico (798 000 [741 000–867 000]), Brazil (792 000 [730 000–847 000]), Indonesia (736 000 [594 000–955 000]), and Pakistan (664 000 [498 000–847 000]). Among these countries, the excess mortality rate was highest in Russia (374·6 deaths [369·7–378·4] per 100 000) and Mexico (325·1 [301·6–353·3] per 100 000), and was similar in Brazil (186·9 [172·2–199·8] per 100 000) and the USA (179·3 [170·7–187·5] per 100 000).

Interpretation: The full impact of the pandemic has been much greater than what is indicated by reported deaths due to COVID-19 alone. Strengthening death registration systems around the world, long understood to be crucial to global public health strategy, is necessary for improved monitoring of this pandemic and future pandemics. In addition, further research is warranted to help distinguish the proportion of excess mortality that was directly caused by SARS-CoV-2 infection and the changes in causes of death as an indirect consequence of the pandemic.
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02796-3/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2821%2902796-3/fulltext)

**title:** Covid-19: Hospital admissions rise as cases increase in over 55s

BMJ| 11th mARCH 2022

England has seen a rise in covid related hospital admissions in the past week, data show. This came as a study showed that covid cases are rising among the over 55s in England, prompting warnings from experts that the pandemic is not over.

Latest hospital data from NHS England show that covid related admissions, which had been declining since the beginning of January, rose by 22% across England in the seven days ending 8 March, from 6894 to 8431.1

Admissions rose in all seven regions of England in the past week. In most areas admissions are still below their January peak, but in the south west, hospital admissions rose 37% (from 878 to 1206) last week and are higher than they were at the peak of the omicron wave. London has seen a 27% increase (801 to 1017) in the past seven days..
<https://www.bmj.com/content/376/bmj.o654>

**title:** Covid-19: Global death toll may be three times higher than official records, study suggests

bmj | 11th mARCH 2022

More than three times as many people may have died worldwide as a result of the covid-19 pandemic than official statistics suggest, according to the first peer reviewed study of global excess deaths.

The research, published in the Lancet, estimates there were 18.2 million excess deaths globally between 1 January 2020 and 31 December 2021 whereas the official death toll was 5.9 million.

The researchers said the mortality impact from the covid-19 pandemic has been “more devastating” than the situation documented by official statistics which provide only a “partial picture” of the true burden of mortality. Evidence from initial studies suggest a significant proportion of excess deaths are a direct result of covid-19, the authors said, but more research is needed.
<https://www.bmj.com/content/376/bmj.o636>

**long-term effects:**

**title:** Covid-19: Studies show lasting cognitive effects after infection

BMJ | 10th mARCH 2022

Two studies published this week have added to a growing body of evidence linking covid infection to subsequent cognitive impairment, even in cases of less severe disease.

One study, a preprint published in Nature,1 examined 785 UK Biobank participants aged 51-81 who routinely receive brain scans and cognitive testing as part of the Biobank’s data gathering. About half of the study population, 401 participants, tested positive for covid after such data were gathered. The remaining 384 control participants did not. In both groups these initial brain scans and cognitive tests were compared with later scans and tests. Participants who had had covid diagnosed showed notably greater changes to the brain, as well as notably greater declines in cognitive scores, than those who did not. This difference remained significant when 15 participants who were admitted to hospital were excluded from the analysis, suggesting that even milder infections are associated with changes to the brain. The changes seen in the previously infected participants included greater reduction in grey matter thickness and tissue contrast in the orbitofrontal cortex and parahippocampal gyrus, greater changes in markers of tissue damage in regions functionally connected to the primary olfactory cortex, and greater reduction in global brain size than was seen in the control group. Persistent effects: Cognitive scores also declined further over the study period in the infected participants than in the control group. The degree of cognitive decline correlated with the extent of physical changes to participants’ brains. The average time from covid diagnosis to the second scan was 141 days, suggesting that negative effects persist for at least four or five months. “Whether this deleterious impact can be partially reversed, or whether these effects will persist in the long term, remains to be investigated with additional follow-up,” the authors wrote. Rebecca Dewey, a senior research fellow in neuroimaging at the University of Nottingham, who was not involved in the research, praised the study’s methodology. “There is a huge advantage from the fact that these people were recruited and scanned before covid was even a thing,” she said. “The same people were then scanned at a later date, and so the changes reported use each person as their own control subject, making the findings really strong.” Alastair Noyce, reader in neurology and neuroepidemiology at Queen Mary University of London, called the analysis “robust.”. “Some of the most striking results relate to involvement of the parts of the brain concerned with olfaction—sense of smell—which is a recognised symptom of covid,” he said. “Earlier studies suggested that covid’s effects on smell were outside the brain, but these results indicate possible changes in the olfactory centres in the brain and changes in connected areas. “I hasten to add that this, as the authors acknowledge, does not mean direct invasion of the brain by covid, and there are several possible explanations. However, it is interesting because a putative mechanism for neurodegenerative diseases is entry via the olfactory structures and then spread to other brain structures.”

Wuhan study: The second study, published in JAMA Neurology,2 followed 1438 covid survivors and 438 uninfected control participants from Wuhan in China, all aged over 60, for a year with cognitive tests at six and 12 months. The study excluded people with pre-existing cognitive impairment, family history of dementia, or serious chronic disease. Rates of cognitive decline were markedly higher in the infected group, particularly in people who had experienced severe covid. In these participants early onset (mild) cognitive decline was 4.87 times more likely than in the uninfected people (95% confidence interval 3.30 to 7.20), and progressive (severe) cognitive decline was 19 times more likely (9.14 to 39.51). Non-severe covid was associated with a 1.71 times higher risk of early onset cognitive decline (1.30 to 2.27). “These findings imply that the pandemic may substantially contribute to the world dementia burden in the future,” the authors warned.
<https://www.bmj.com/content/376/bmj.o640>

**title:** One-Year Trajectory of Cognitive Changes in Older Survivors of COVID-19 in Wuhan, China: A Longitudinal Cohort Study

JAMA |8th march 2022

Question What is the dynamic trajectory of cognitive changes in the elderly population surviving COVID-19? Findings In this cohort study of 1438 COVID-19 survivors 60 years and older who were discharged from COVID-19–designated hospitals in Wuhan, China, the incidence of cognitive impairment was higher in COVID-19 survivors, especially those with severe cases, compared with uninfected participants during a 1-year follow-up period. Meaning The findings suggest that long-term cognitive decline is common after SARS-CoV-2 infection, indicating the necessity of evaluating the impact of the COVID-19 pandemic on the future dementia burden worldwide.
<https://jamanetwork.com/journals/jamaneurology/fullarticle/2789919>

**VACCINATION & infection control**

**title:** Clinical severity of, and effectiveness of mRNA vaccines against, covid-19 from omicron, delta, and alpha SARS-CoV-2 variants in the United States: prospective observational study

bmj |9th march 2022

Objectives To characterize the clinical severity of covid-19 associated with the alpha, delta, and omicron SARS-CoV-2 variants among adults admitted to hospital and to compare the effectiveness of mRNA vaccines to prevent hospital admissions related to each variant. Design Case-control study. Setting 21 hospitals across the United States. Participants 11 690 adults (≥18 years) admitted to hospital: 5728 with covid-19 (cases) and 5962 without covid-19 (controls). Patients were classified into SARS-CoV-2 variant groups based on viral whole genome sequencing, and, if sequencing did not reveal a lineage, by the predominant circulating variant at the time of hospital admission: alpha (11 March to 3 July 2021), delta (4 July to 25 December 2021), and omicron (26 December 2021 to 14 January 2022).

Main outcome measures Vaccine effectiveness calculated using a test negative design for mRNA vaccines to prevent covid-19 related hospital admissions by each variant (alpha, delta, omicron). Among patients admitted to hospital with covid-19, disease severity on the World Health Organization’s clinical progression scale was compared among variants using proportional odds regression.

Results Effectiveness of the mRNA vaccines to prevent covid-19 associated hospital admissions was 85% (95% confidence interval 82% to 88%) for two vaccine doses against the alpha variant, 85% (83% to 87%) for two doses against the delta variant, 94% (92% to 95%) for three doses against the delta variant, 65% (51% to 75%) for two doses against the omicron variant; and 86% (77% to 91%) for three doses against the omicron variant. In-hospital mortality was 7.6% (81/1060) for alpha, 12.2% (461/3788) for delta, and 7.1% (40/565) for omicron. Among unvaccinated patients with covid-19 admitted to hospital, severity on the WHO clinical progression scale was higher for the delta versus alpha variant (adjusted proportional odds ratio 1.28, 95% confidence interval 1.11 to 1.46), and lower for the omicron versus delta variant (0.61, 0.49 to 0.77). Compared with unvaccinated patients, severity was lower for vaccinated patients for each variant, including alpha (adjusted proportional odds ratio 0.33, 0.23 to 0.49), delta (0.44, 0.37 to 0.51), and omicron (0.61, 0.44 to 0.85).

Conclusions: mRNA vaccines were found to be highly effective in preventing covid-19 associated hospital admissions related to the alpha, delta, and omicron variants, but three vaccine doses were required to achieve protection against omicron similar to the protection that two doses provided against the delta and alpha variants. Among adults admitted to hospital with covid-19, the omicron variant was associated with less severe disease than the delta variant but still resulted in substantial morbidity and mortality. Vaccinated patients admitted to hospital with covid-19 had significantly lower disease severity than unvaccinated patients for all the variants.
<https://www.bmj.com/content/376/bmj-2021-069761>

**title:** Safety of mRNA vaccines administered during the initial 6 months of the US COVID-19 vaccination programme: an observational study of reports to the Vaccine Adverse Event Reporting System and v-safe

the lancet infectious diseases| 7th march 2022

Background. In December, 2020, two mRNA-based COVID-19 vaccines were authorised for use in the USA. We aimed to describe US surveillance data collected through the Vaccine Adverse Event Reporting System (VAERS), a passive system, and v-safe, a new active system, during the first 6 months of the US COVID-19 vaccination programme. Methods: In this observational study, we analysed data reported to VAERS and v-safe during Dec 14, 2020, to June 14, 2021. VAERS reports were categorised as non-serious, serious, or death. Reporting rates were calculated using numbers of COVID-19 doses administered as the denominator. We analysed v-safe survey reports from days 0–7 after vaccination for reactogenicity, severity (mild, moderate, or severe), and health impacts (ie, unable to perform normal daily activities, unable to work, or received care from a medical professional).

Findings: During the study period, 298 792 852 doses of mRNA vaccines were administered in the USA. VAERS processed 340 522 reports: 313 499 (92·1%) were non-serious, 22 527 (6·6%) were serious (non-death), and 4496 (1·3%) were deaths. Over half of 7 914 583 v-safe participants self-reported local and systemic reactogenicity, more frequently after dose two (4 068 447 [71·7%] of 5 674 420 participants for local reactogenicity and 4 018 920 [70·8%] for systemic) than after dose one (4 644 989 [68·6%] of 6 775 515 participants for local reactogenicity and 3 573 429 [52·7%] for systemic). Injection-site pain (4 488 402 [66·2%] of 6 775 515 participants after dose one and 3 890 848 [68·6%] of 5 674 420 participants after dose two), fatigue (2 295 205 [33·9%] participants after dose one and 3 158 299 participants [55·7%] after dose two), and headache (1 831 471 [27·0%] participants after dose one and 2 623 721 [46·2%] participants after dose two) were commonly reported during days 0–7 following vaccination. Reactogenicity was reported most frequently the day after vaccination; most reactions were mild. More reports of being unable to work, do normal activities, or of seeking medical care occurred after dose two (1 821 421 [32·1%]) than after dose one (808 963 [11·9%]); less than 1% of participants reported seeking medical care after vaccination (56 647 [0·8%] after dose one and 53 077 [0·9%] after dose two).

Interpretation: Safety data from more than 298 million doses of mRNA COVID-19 vaccine administered in the first 6 months of the US vaccination programme show that most reported adverse events were mild and short in duration.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00054-8/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900054-8/fulltext)

**title:** COVID-19 mRNA vaccine safety during the first 6 months of roll-out in the USA [comment]

the lancet infectious diseases | 7th march 2022

…Despite these limitations, with the VAERS, v-safe, and vaccine administration data, the safety monitoring of the mRNA COVID-19 vaccines stands out as the most comprehensive of any vaccine in US history. The use of these complementary monitoring systems has provided robust and reassuring data on the epidemiology of adverse events related to mRNA COVID-19 vaccines that reinforce the importance of both continued surveillance and safety of COVID-19 immunisation and support continued confidence in vaccinationc funding given to companies for future vaccine development should have global access.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00123-2/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900123-2/fulltext)

**title:** Hypersensitivity Reactions to COVID-19 Vaccines—Identify High-Risk Children and Vaccinate the Rest

jama pediatrics| 7th march 2022

COVID-19 vaccines are highly effective in preventing severe COVID-19 disease and hospitalization in adults and adolescents aged 12 to 15 years.1 Recently, the BNT162b2 (Pfizer-BioNTech) vaccine was granted emergency use authorization for children aged 5 to 11 years, and the vaccine has shown to be 90.7% effective in preventing symptomatic COVID-19 in children of this age group. Although highly efficacious in preventing COVID-19 disease, hypersensitivity reactions associated with the COVID-19 vaccines have been reported since the December 2020 vaccine rollout. To date, the pooled prevalence of COVID-19 vaccine hypersensitivity reactions is an estimated 5.58 cases per million doses administered.2 Although these hypersensitivity reactions are rare, with the current rollout of COVID-19 vaccine emergency use authorization for children aged 5 to 11 years it will be more important for the pediatric medical community to (1) recognize who is at risk of COVID-19 vaccine hypersensitivity reactions and (2) distinguish who should receive additional COVID-19 vaccine doses after a reaction from those who should be referred to an allergist.
<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2789414>

**title:** Secondary Attack Rates for Omicron and Delta Variants of SARS-CoV-2 in Norwegian Households

JAMA| 7th march 2022

Secondary attack rate of SARS-CoV-2 in Norwegian households was moderately higher when the index case had the Omicron variant rather than the Delta variant. … A strength of the study is the use of nationwide individual-level household data from mandatory reporting on all PCR tests in Norway. A limitation is that data on home tests were not available, and that test activity differed between groups. However, the national regulation prescribed that all positive-result home tests be confirmed by a PCR test, and this is also required to obtain an immunity certificate. Thus, most positive test results are probably recorded. Some Omicron cases could go undetected because of milder symptoms. Sampling for variant analysis of index cases was not random, but similar results for Delta and nonclassified variants suggest that selection bias was limited. Also, household members may have been infected by a third-party source, but such potential bias should be similar across variants.
<https://jamanetwork.com/journals/jama/fullarticle/2789920>

**title:** Transmission of SARS-CoV-2 delta variant (AY.127) from pet hamsters to humans, leading to onward human-to-human transmission: a case study

the lancet | 12th march 2022

Background: Transmission of SARS-CoV-2 from humans to other mammals, including pet animals, has been reported. However, with the exception of farmed mink, there is no previous evidence that these infected animals can infect humans, resulting in sustained human-to-human transmission. Following a confirmed SARS-CoV-2 infection of a pet shop worker, animals in the shop and the warehouse supplying it were tested for evidence of SARS-CoV-2 infection.

Methods: In this case study, viral swabs and blood samples were collected from animals in a pet shop and its corresponding warehouse in Hong Kong. Nasal swab or saliva samples from human COVID-19 patients epidemiologically linked to the pet shop and from subsequent local cases confirmed to be infected by SARS-CoV-2 delta variant were collected. Oral swabs were tested by quantitative RT-PCR (RT-qPCR) for SARS-CoV-2 and blood samples were serologically tested by a surrogate virus neutralisation test and plaque reduction neutralisation test. The SARS-CoV-2 RT-qPCR positive samples were sequenced by next generation viral full genome sequencing using the ISeq sequencing platform (Illumina), and the viral genomes were phylogenetically analysed.

Findings: Eight (50%) of 16 individually tested Syrian hamsters in the pet shop and seven (58%) of 12 Syrian hamsters in the corresponding warehouse were positive for SARS-CoV-2 infection in RT-qPCR or serological tests. None of the dwarf hamsters (n=75), rabbits (n=246), guinea pigs (n=66), chinchillas (n=116), and mice (n=2) were confirmed positive for SARS-CoV-2 in RT-qPCR tests. SARS-CoV-2 viral genomes deduced from human and hamster cases in this incident all belong to the delta variant of concern (AY.127) that had not been circulating locally before this outbreak. The viral genomes obtained from hamsters were phylogenetically related with some sequence heterogeneity. Phylogenetic dating suggests infection in these hamsters occurred around Oct 14, 2021 (95% CI Sept 15 to Nov 9, 2021). Multiple zoonotic transmission events to humans were detected, leading to onward human-to-human transmission.

Interpretation: Pet hamsters can be naturally infected with SARS-CoV-2. The virus can circulate among hamsters and lead to human infections. Both genetic and epidemiological results strongly suggest that there was more than one hamster-to-human transmission event in this study. This incident also led to onward human transmission. Importation of SARS-CoV-2-infected hamsters was a likely source of this outbreak.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2119451>

**title:** Spreading of SARS-CoV-2 from hamsters to humans [comment]

the lancet| 12th march 2022

The Article in The Lancet by Hui-Ling Yen and colleagues now adds another species to the list, providing evidence that pet hamsters can be naturally infected with SARS-CoV-2 and cause human infections. Both the genetic and epidemiological results reported here strongly suggest that there were several hamster-to-human transmission events, followed by onward human transmission. The authors report that Syrian hamsters at a warehouse and two pet shops supplied by this warehouse in Hong Kong had evidence of SARS-CoV-2 infection. Two patients were infected with SARS-CoV-2 directly from infected hamsters in one of the pet shops. Based on the genetic and phylogentic analysis of the viruses, local transmission of SARS-CoV-2 leading to infection of hamsters in the warehouse seemed unlikely. Importation of SARS-CoV-2-infected hamsters on the other hand, from the Czech Republic via the Netherlands to Hong Kong, was a likely source of this outbreak, say the authors. However, further in-depth outbreak investigation would be needed to find out whether the hamsters were infected during transport or at the animal facilities. Reported separately, a second strain was found in some animals in the warehouse, showing that the infection of the hamsters was not a one-off incident. .. This zoonotic transmission of SARS-CoV-2 from hamsters is consistent with experimental observations of efficient hamster-to-hamster transmission via different routes.
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00423-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2900423-8/fulltext)

**title:** Maintaining face mask use before and after achieving different COVID-19 vaccination coverage levels: a modelling study

the lancet public health| 8th march 2022

Background. Face mask wearing has been an important part of the response to the COVID-19 pandemic. As vaccination coverage progresses in countries, relaxation of such practices is increasing. Subsequent COVID-19 surges have raised the questions of whether face masks should be encouraged or required and for how long. Here, we aim to assess the value of maintaining face masks use indoors according to different COVID-19 vaccination coverage levels in the USA.

Methods: In this computational simulation-model study, we developed and used a Monte Carlo simulation model representing the US population and SARS-CoV-2 spread. Simulation experiments compared what would happen if face masks were used versus not used until given final vaccination coverages were achieved. Different scenarios varied the target vaccination coverage (70–90%), the date these coverages were achieved (Jan 1, 2022, to July 1, 2022), and the date the population discontinued wearing face masks.

Findings: Simulation experiments revealed that maintaining face mask use (at the coverage seen in the USA from March, 2020, to July, 2020) until target vaccination coverages were achieved was cost-effective and in many cases cost saving from both the societal and third-party payer perspectives across nearly all scenarios explored. Face mask use was estimated to be cost-effective and usually cost saving when the cost of face masks per person per day was ≤US$1·25. In all scenarios, it was estimated to be cost-effective to maintain face mask use for about 2–10 weeks beyond the date that target vaccination coverage (70–90%) was achieved, with this added duration being longer when the target coverage was achieved during winter versus summer. Factors that might increase the transmissibility of the virus (eg, emergence of the delta [B.1.617.2] and omicron [B.1.1.529] variants), or decrease vaccine effectiveness (eg, waning immunity or escape variants), or increase social interactions among certain segments of the population, only increased the cost savings or cost-effectiveness provided by maintaining face mask use.

Interpretation: Our study provides strong support for maintaining face mask use until and a short time after achieving various final vaccination coverage levels, given that maintaining face mask use can be not just cost-effective, but even cost saving. The emergence of the omicron variant and the prospect of future variants that might be more transmissible and reduce vaccine effectiveness only increases the value of face masks.
[https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(22)00040-8/fulltext](https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667%2822%2900040-8/fulltext)

**title:** Emerging evidence on heterologous COVID-19 vaccine schedules—To mix or not to mix?

the lancet infectious diseases| 9th march 2022

We did a comprehensive review of available data on the safety, immunogenicity, and effectiveness of heterologous vaccine schedules (for methods, see appendix pp 1–3). We identified 48 studies that tested a combination of WHO EUL COVID-19 vaccines from different platforms. These included seven controlled trials and 41 observational studies. Schedules involved a combination (in any order) of vectored–mRNA vaccines (36 studies), vectored–inactivated vaccines (eight studies), and inactivated–mRNA vaccines (eight studies). No protein-based vaccines had received a WHO EUL at the time of the review. A total of 37 studies considered heterologous primary schedules (involving more than one product during a two-dose primary series), whereas 13 considered heterologous boosting (among individuals who have previously received a complete homologous primary series). Most studies considered humoral immune response endpoints (38 studies), with a subset reporting on safety (23 studies) and vaccine effectiveness (VE; 11 studies)….

… Heterologous schedules are poised to play an increasingly important role within the global COVID-19 vaccine strategy. In part, this will be driven by pragmatism as countries contend with variable supply for different vaccine products. However, independent of access considerations, the emerging VE and immunogenicity data highlight the value of heterologous schedules, depending on the platforms involved and the order of products used. A flexible approach to heterologous schedules is warranted as we seek to make optimal use of a diverse vaccine portfolio.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00178-5/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900178-5/fulltext)

**title:** Immunogenicity and Reactogenicity of Vaccine Boosters after Ad26.COV2.S Priming

new england journal of medicine| 10th march 2022

The Ad26.COV2.S vaccine, which was approved as a single-shot immunization regimen, has been shown to be effective against severe coronavirus disease 2019. However, this vaccine induces lower severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein (S)–specific antibody levels than those induced by messenger RNA (mRNA)–based vaccines. The immunogenicity and reactogenicity of a homologous or heterologous booster in persons who have received an Ad26.COV2.S priming dose are unclear…

The Ad26.COV2.S and mRNA boosters had an acceptable safety profile and were immunogenic in health care workers who had received a priming dose of Ad26.COV2.S vaccine. The strongest responses occurred after boosting with mRNA-based vaccines. Boosting with any available vaccine was better than not boosting.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2116747>

**title:** Covid-19: Coalition pledges $42m to develop broad protection vaccine against betacoronaviruses

BMJ| 9th march 2022

The Coalition for Epidemic Preparedness Innovations (CEPI) has pledged up to $42m to support the development of a vaccine that could provide broad protection against SARS-CoV-2 as well as other betacoronaviruses including severe acute respiratory syndrome and Middle East respiratory syndrome.

The vaccine development is being led by biotech company DIOSynVax—which came out of the University of Cambridge. Unlike most other covid-19 vaccines, DIOSynVax is not focusing on the SARS-CoV-2 spike protein as this is vulnerable to mutation. Instead, it is looking at the whole family of coronaviruses to target areas that cannot mutate without the viruses dying or impairing their own ability to replicate.

If successful, the team will produce an antigen structure made from multiple synthetic antigens—known as a vaccine antigen payload—that can then be delivered using different vaccine vectors, such as mRNA, adenovirus, and protein based platforms.

The funding was announced at the Global Pandemic Preparedness Summit in London on 8 March, which was co-hosted by CEPI and the UK government. As part of the funding agreement, DIOSynVax has committed to achieving equitable access, in line with CEPI’s equitable access policy.2
<https://www.bmj.com/content/376/bmj.o628>

**title:** We need to optimise genome surveillance and tracing of SARS-CoV-2 variants [letter]

BMJ| 11th march 2022

…Detection of SGTF seemed to be an effective strategy to contain omicron through targeted contact tracing and isolation, but the rapid evolution of variants and sub-lineages, and the unfolding data regarding their genetic profiles, need to be incorporated into our diagnostics tools if we are to succeed in overcoming SARS-CoV-2.
<https://www.bmj.com/content/376/bmj.o601>

**title:** Effect of mRNA Vaccine Boosters against SARS-CoV-2 Omicron Infection in Qatar

new england journal of medicine | 9th march 2022

Waning of vaccine protection against coronavirus disease 2019 (Covid-19) and the emergence of the omicron (or B.1.1.529) variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have led to expedited efforts to scale up booster vaccination. Protection conferred by booster doses of the BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna) vaccines in Qatar, as compared with protection conferred by the two-dose primary series, is unclear.

Methods: We conducted two matched retrospective cohort studies to assess the effectiveness of booster vaccination, as compared with that of a two-dose primary series alone, against symptomatic SARS-CoV-2 infection and Covid-19–related hospitalization and death during a large wave of omicron infections from December 19, 2021, through January 26, 2022. The association of booster status with infection was estimated with the use of Cox proportional-hazards regression models….

…The messenger RNA (mRNA) boosters were highly effective against symptomatic delta infection, but they were less effective against symptomatic omicron infection. However, with both variants, mRNA boosters led to strong protection against Covid-19–related hospitalization and death.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2200797>

**title:** Increasing vaccine uptake . . . and other stories

BMJ| 10th march 2022

Journalists and politicians use the phrase “vaccine hesitancy” to explain why people remain un-immunised despite plentiful supplies of vaccine. The term misleadingly implies that responsibility for a successful vaccination programme lies with individuals. In fact, it is governments that have the power to make vaccines accessible and acceptable. A discussion in Nature (https://www.nature.com/articles/d41586-022-00495-8) gives pre-pandemic examples of how policy changes (such as developing appropriate messaging and ensuring vaccine availability) have a strong influence on vaccination rates.
<https://www.bmj.com/content/376/bmj.o558.full>

**title:** COVID-19 vaccination challenge: what have we learned from the Brazilian process?

the lancet global health| 10th march 2022

Despite a long tradition of strong primary health-care systems, some Latin American countries—such as Brazil and Mexico—have suffered the worst during the pandemic. Political denialism and conflict, lack of resources, and weak institutional contexts within federalised systems can account for high case numbers and mortality within these countries. However, towards the end of 2021, Latin America had some of the highest vaccination coverage in the world. The EU had reached a vaccination coverage of approximately 74·3% of the total population with at least one dose as of Feb 12, 2022, yet such statistics mask the vast differences between member states, ranging from 93·6% in Portugal to only 29·8% of the population in Bulgaria. In some African countries, vaccination remains the privilege of a very small minority. How has Brazil, a Latin American country that had so many problems during the initial years of the pandemic, had such success in its vaccine programmes, with a vaccination coverage of 83% (one dose)?
[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00049-3/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X%2822%2900049-3/fulltext)

**title:** COVID-19 vaccine coverage and factors associated with vaccine uptake among 23 247 adults with a recent history of homelessness in Ontario, Canada: a population-based cohort study

the lancet public health| 9th march 2022

People experiencing homelessness face a high risk of SARS-CoV-2 infection and transmission, as well as health complications and death due to COVID-19. Despite being prioritised for receiving the COVID-19 vaccine in many regions, little data are available on vaccine uptake in this vulnerable population. Using population-based health-care administrative data from Ontario, Canada—a region with a universal, publicly funded health system—we aimed to describe COVID-19 vaccine coverage (ie, the estimated percentage of people who have received a vaccine) and determinants of vaccine receipt among individuals with a recent history of homelessness.
[https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(22)00037-8/fulltext](https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667%2822%2900037-8/fulltext)

**title:** Expanding Efforts and Support to Respond to the HIV and COVID-19 Intersecting Pandemics

Jama| 11th march 2022

Considerable inferential data indicate that immunocompromised persons with persistent COVID-19 infection may be involved in the generation of SARS-CoV-2 variants of concern globally.1-3 The largest immunocompromised population worldwide is people living with HIV. Although tremendous gains have been made in providing access to lifesaving antiretroviral therapy, only approximately 50% of the estimated 37.7 million people living with HIV globally are optimally treated.4 The emergence of the SARS-CoV-2 Omicron variant is a stark illustration of the intersecting COVID-19 and HIV pandemics, highlighting the interrelationships and detrimental effects each of these infectious diseases has on the other.5 HIV infection is a risk factor for increased mortality from COVID-19, even more so when HIV is not controlled by antiretroviral therapy,6 and emerging data suggest that immunosuppression may be facilitating the development of SARS-CoV-2 variants of concern…
<https://jamanetwork.com/journals/jama/fullarticle/2790239>

**title:** Antigen vs RT-PCR Tests for Screening Quarantined Students in Florida During the COVID-19 Pandemic SARS-CoV-2 Delta Variant Surg

jama pediatrics | 7th march 2022

In the US, schools opened in fall 2021 during a surge of COVID-19 cases attributed to the SARS-CoV-2 Delta variant.1 The US Centers for Disease Control and Prevention recommended masking in schools and return to school of asymptomatic quarantined close contacts at day 7 after the last date of SARS-CoV-2 exposure with a negative test result or at day 10 without a test. Rapid antigen tests have been proposed as a tool to reduce or even eliminate quarantine,2 but there are uncertainties about their performance compared with real-time reverse transcription–polymerase chain reaction (RT-PCR) tests.3-5 Most validation studies on these tests were done before the Delta variant emerged, which may impact results because of the variant’s higher viral load.6 The aim of this study was to assess whether rapid antigen and RT-PCR tests gave comparable results and whether antigen testing on day 5 after SARS-CoV-2 exposure would be helpful in making decisions about when quarantined children can return to school.
<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2789417>

**title:** Meeting the Moment by Vaccinating Prison Staff Against COVID-19

JAMA | 11th march 2022

People in carceral settings have been disproportionately affected by COVID-19 in terms of the sheer volume of cases, hospitalizations, and deaths.1,2 Evidence-based strategies to mitigate the risk of viral transmission, including masking, testing, and disinfecting, were slowly and unevenly implemented across prisons, compounding inherent risks associated with overcrowded conditions in congregate settings. In the absence of well-deployed infection prevention measures, the COVID-19 pandemic revealed a pressing need for vaccinating prison staff to: (1) reduce staff morbidity and mortality; (2) reduce staff absenteeism because of isolation/quarantine that can disrupt facility operations; and (3) reduce onward transmission to the vulnerable residents of facilities and the communities where staff live. To date, few carceral systems have provided transparent comprehensive data on staff vaccination that would answer the following question: how successfully has vaccination rolled out among prison staff who interface with residents? This type of data is needed to identify gaps and inform the next stages of vaccine implementation.
<https://jamanetwork.com/journals/jama-health-forum/fullarticle/2789955>

**title:** Humoral Responses Against Variants of Concern by COVID-19 mRNA Vaccines in Immunocompromised Patients

jama oncology | 10th march 2022

Question Are there differences in the magnitude and durability of neutralizing antibody (nAb) responses against SARS-CoV-2 variants of concern (VOCs) according to the mRNA-1273 (Moderna) and BNT162b2 (Pfizer-BioNTech) vaccines?

Findings In this comparative effectiveness study of 637 immunocompromised patients and 204 healthy control participants who received 2 doses of messenger RNA COVID-19 vaccines, nAb responses against the Beta and Delta variants were short lived (3 to 7 months) compared with original, nonvariant SARS-CoV-2 and other variants. Higher nAb titers and longer durability of humoral responses were associated with vaccination with the mRNA-1273 vaccine.

Meaning The faster disappearance of the nAb responses in certain groups of immunocompromised patients suggests that boosting vaccine strategies need to be personalized to the underlying disease.
<https://jamanetwork.com/journals/jamaoncology/fullarticle/2790203>

**title:** Evaluation of Antibody Response to SARS-CoV-2 mRNA-1273 Vaccination in Patients With Cancer in Florida

jama oncology | 10th march 2022

Question Does the immune response to the mRNA-1273 vaccine differ among patients with solid tumors and hematologic cancer?

Findings In this cohort study of 515 patients with cancer, seropositivity after the first and second vaccine doses was 71% and 90%, respectively. Antibody levels after vaccination were substantially higher among patients who were seropositive before vaccination.

Meaning Results of this study suggest that the mRNA-1273 vaccine induced a highly variable seroconversion percentage among patients with cancer; these patients may benefit from additional vaccine doses.
<https://jamanetwork.com/journals/jamaoncology/fullarticle/2790099>

**title:** Safety and immunogenicity of a synthetic multiantigen modified vaccinia virus Ankara-based COVID-19 vaccine (COH04S1): an open-label and randomised, phase 1 trial

the lancet | 9th march 2022

…COH04S1 was well tolerated and induced spike-specific and nucleocapsid-specific antibody and T-cell responses. Future evaluation of this COVID-19 vaccine candidate as a primary or boost vaccination is warranted.
[https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(22)00027-1/fulltext](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247%2822%2900027-1/fulltext)

**title:** COMPARISON OF SEROCONVERSION IN CHILDREN AND ADULTS WITH MILD COVID-19

jama | 9th march 2022

Question What proportion of children with mild SARS-CoV-2 infection undergo seroconversion compared with adults?

Findings In this cohort study of 57 children and 51 adults, the proportion of children with seroconversion to SARS-CoV-2 was half that found in adults despite similar viral load.

Meaning These findings suggest that serology may provide a less reliable marker of prior SARS-CoV-2 infection in children and support strategies to protect children against COVID-19, including vaccination.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2789845>

**workforce well-being**

**title:** Solving retention to support workforce recovery post-pandemic

BMJ | 9th march 2022

The covid-19 pandemic has stretched healthcare staff like never before. As part of the 2022 Nuffield Trust summit, The BMJ hosted a roundtable discussion looking at why workers leave the NHS and how staff wellbeing and retention can be improved. Tom Moberly reports.
<https://www.bmj.com/content/376/bmj.o578>

**title:** NHS Pension Scheme: Proposed Amendments To Continue The Suspension Of Restrictions On Return To Work Introduced By The Coronavirus Act 2020 (Section 45) – Response To Consultation

DHSC| 10th march 2022

This consultation response sets out the continuation of retire and return easements in the NHS pension scheme which will take effect immediately following the expiry of Section 45 of the Coronavirus Act (2020). It also confirms that these temporary easements will run to 31 October 2022.
<https://kingsfund.blogs.com/health_management/2022/03/nhs-pension-scheme-proposed-amendments-to-continue-the-suspension-of-restrictions-on-return-to-work-.html>

**recovery: HEALTH MANgement, services & Education**

**title:** virtual wards

institute of health & social care management | 10th march 2022

This report discusses virtual wards, an innovation due to be implemented at scale in the NHS as a method of addressing patient waiting lists. With the help of remote treatment options and supported by technology, patients are monitored and cared for, in their own homes. The report lists the advantages and disadvantages of this approach.
<https://kingsfund.blogs.com/health_management/2022/03/virtual-wards.html>

**title:** We can live with covid, but that doesn’t have to mean living with avoidable deaths and disability [opinion]

BMJ | 10th march 2022

…The peak of omicron may be just passing, but deaths in the UK have remained at a plateau since the start of the year and are still averaging around 100 a day.8 The number of people testing positive for covid-19 is climbing and on 9 March 2022, more than 60 000 people had a positive test result.8 It is still adding to hospital activity, which is exhausting for healthcare staff, and which prevents other treatments being done, adding to the ever growing backlog of elective care. The vaccination programme has all but ground to a halt,9 even though around a third of UK adults haven’t had a booster dose. Even with a fully vaccinated population, we are not sure of how waning vaccine efficacy may play out.

The announcement of all restrictions ending creates the message that covid-19 has all but disappeared when it has clearly not. Suggestions in many countries that isolation periods be reduced—and now, indeed, the abolition of the legal requirement to self-isolate altogether in England—threaten to allow a second spike of omicron infections, putting vulnerable adults at further risk.

“Living with covid” means recognising that what we previously called “restrictions” should be called “protections.” The language of “freedom” and “removing restrictions” leaves the country unprepared for the next potential wave. Certain behaviours that people adopted and governments mandated during the first waves of the pandemic can still be helpful, and should be kept, to protect our health in winter in the future—whether from covid-19 or other respiratory viruses. These include working from home when possible, washing hands more frequently, wearing a well fitting N95/FFP2 mask in crowded and indoor public spaces, improving indoor air quality, and still enabling remote healthcare consultations.

It’s also vital that we leave behind a culture of presenteeism. Whether it is flu or any other respiratory virus, no one should go to work or feel pressured to if they are ill….
<https://www.bmj.com/content/376/bmj.o638>

**title:** Shifting tides: reflecting on medical education in the time of covid-19

bmj | 11th march 2022

Covid-19 has highlighted the flaws in our healthcare systems, but also helped imagine a better, writes Monica Cheng. It was a cool January evening when I plugged in my headphones and plunged into the virtual meeting room. As nightfall descended outside, I found myself transported to the terraced steps of a brightly lit conference building where night and day ceased to exist and medical students across the country engaged in a residency interview season that resembled none other.

During the covid-19 pandemic, we have borne witness to the toll the virus has taken on our minds and bodies and the cost of heroism that has become expected of healthcare workers who navigate the complexities of an imperfect healthcare system and its intersection with society and medicine. As traditional structures of medical training were disrupted and the residency selection cycle pivoted to a virtual format, medical students have been placed in a unique position to measure and reflect on ways to add value to a new generation of healthcare.
<https://www.bmj.com/content/376/bmj.o657>

**title:** We cannot afford to repeat these four pandemic mistakes

BMJ | 10th march 2022

Many countries are declaring an end to this phase of the covid-19 pandemic, yet the underlying weaknesses that hampered our response remain unsolved, says Abraar Karan

As a physician, one of the hardest parts of the covid-19 pandemic was watching patients get steadily sicker and often die. At the bedside, we see past the numbers dispassionately presented on data dashboards and instead understand the real human suffering that is at the heart of a virus like SARS-CoV-2 spreading. I have also had the unique experience of working on a state pandemic response with leading decision makers; as such, I was a witness to the complex policy tradeoffs involved in trying to control a pandemic. There are always winners and losers in these decisions. Yet when we pull back on public health protections, the ensuing harms are more heavily burdened on those who often are not in a position to adequately protect themselves. As healthcare workers, they often end up as our patients—and their stories offer examples of where our pandemic response failed. As the US joins other countries in declaring an end to this phase of the pandemic, marked by the rolling back of important guidance, including indoor masking, I am left with concerns for our future pandemic preparedness for a few key reasons.
<https://www.bmj.com/content/376/bmj.o631>

**title:** The COVID-19 Pandemic Strikes Again and Again and Again

JAMA | 9th march 2022

The COVID-19 pandemic has proven relentlessly challenging for health care. Although some positive consequences have resulted from these challenges, including the move to routine virtual health care and the increased attention on staffing and supply chain sustainability, these positive consequences have been overwhelmed by the pandemic’s negative impacts on health. Dang et al1 tally yet one more adverse outcome of COVID-19: among Medicare patients, mortality after hospitalization for non–COVID-19 diagnoses increased significantly. In a retrospective study of more than 8.4 million Medicare admissions between January 2019 and September 2021 occurring at 4626 US hospitals, 30-day risk-adjusted mortality among patients without COVID-19 increased by more than 20%, from 9.43% before COVID-19 to 11.48% after COVID-19.

 Perhaps the most striking finding from the study1 was that increased mortality was observed in hospitals with more COVID-19–related admissions, confirming the far-reaching consequences of COVID-19–related strain on the health care system. Strain, which is defined as nearing or exceeding the limits of the care team’s ability to provide high-quality care to all patients who require it,2 is a phenomenon that is intimately familiar to clinicians during COVID-19 but that can be challenging to quantify and study. Strain is typically measured through metrics of how busy the hospital is, such as occupancy, acuity, turnover, admissions, discharges, and/or the need for organ support therapy.3 Prior work3 has shown that during periods of high hospital strain, borderline patients with common illnesses like sepsis and acute respiratory failure are far less likely to be admitted to the intensive care unit compared with periods of low strain. This is a stark example of how strain can impact routine care processes and even patient outcomes in severe illness.

The COVID-19 pandemic has strained health systems around the world in unprecedented ways, with all health systems grappling with limitations in staffing (physicians, nurses, respiratory therapists, and pharmacists), supplies (medications, tests, ventilators, high-flow oxygen machines, and vaccines), and space (hospital beds, subacute nursing facility beds, and dialysis units). During the pandemic’s inpatient surges, COVID-19–specific mortality was already known to increase.4 However, the study by Dang et al1 confirms a lingering concern that clinicians have feared might also be true: elderly patients admitted to hospitals with diagnoses other than COVID-19 are more likely to die during surges, even after adjusting for patient and hospital characteristics. This work is important because it quantifies a very serious source of harm that is not part of the daily COVID-19 case or death counts highlighted in the media…
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2789848>

**title:** Impact Of Covid-19 On New Parents: One Year On: Government Response To The Committee’s First Report

house of commons petitions committee | 9th march 2022

The original report, Impact of Covid-19 on new parents: one year on, was published in October 2021, and followed the Committee’s inquiry and first report in 2020 into the impact of Covid-19 on new parents. In July 2021, a year on from the publication of its first report, the Committee took further evidence from campaigners and experts to assess progress against the recommendations made in the report. The Government’s response points to the £500 million investment announced in the 2021 Autumn Spending Review for family and early years services. This report concludes that this goes some way to addressing the ‘baby blind spot’ in Covid-19 recovery spending identified in the Committee’s report but the response contains no new commitments in response to the concerns raised and recommendations made in the report.
<https://kingsfund.blogs.com/health_management/2022/03/impact-of-covid-19-on-new-parents-one-year-on-government-response-to-the-committees-first-report.html>

**title:** One Hundred Million Cases In One Hundred Week: Working Towards Better Covid-19 Outcomes In The WHO European Region

who europe | 11th march 2022

This report showcases the work of WHO/Europe’s Covid-19 Incident Management Support Team (IMST) – the mechanism activated to deal with emergency situations – from its establishment in early 2020, as the first cases of Covid-19 were being detected in the European Region, to 2022. It also includes insights into the work of the operational teams during this time as they supported some of the Region’s Member States in dealing with the challenges of a global pandemic. It details the work and the impact of its Covid-19 responses across various functions, including surveillance, public health and social measures, risk communication and community engagement, clinical and health interventions, essential health services, and vaccines.
<https://kingsfund.blogs.com/health_management/2022/03/one-hundred-million-cases-in-one-hundred-week-working-towards-better-covid-19-outcomes-in-the-who-eu.html>

**HEALTH INEQUALITIES**

**title:** Covid-19: Pandemic has shown that science can widen inequalities, says WHO head

BMJ |11th march 2022

The covid-19 pandemic has been exacerbated by underinvestment in public health, an “infodemic” of false or misleading information, and a deficit of trust, the director general of the World Health Organization has said.

Speaking at the Global Pandemic Preparedness Summit in London on 8 March, co-hosted by the Coalition for Epidemic Preparedness Innovations (CEPI) and the UK government, Tedros Adhanom Ghebreyesus said that the past two years had shown how “science can actually serve to widen inequalities rather than narrow them,” as shown by the huge inequity in distribution of vaccines and diagnostic testing.

As of 10 March only 13.7% of people in low income countries had received at least one dose of a covid-19 vaccine.1 “It has become obvious that equity cannot be left to market forces or goodwill or shifting geopolitical currents,” said Tedros…
<https://www.bmj.com/content/376/bmj.o644>

**title:** Racial and Ethnic, Gender Disparities Seen in LGBT COVID-19 Vaccination Rates

JAMA | 8th MARCH 2022

Compared with heterosexual adults, a greater proportion of gay and lesbian adults reported having received at least 1 dose of COVID-19 vaccine, according to a report on results from a nationally representative telephone survey. By race and ethnicity, however, vaccination rates were lowest among Black lesbian, gay, bisexual, and transgender (LGBT) individuals, particularly women. ompared with heterosexual adults, a greater proportion of gay and lesbian adults reported having received at least 1 dose of COVID-19 vaccine, according to a report on results from a nationally representative telephone survey. By race and ethnicity, however, vaccination rates were lowest among Black lesbian, gay, bisexual, and transgender (LGBT) individuals, particularly women.
<https://jamanetwork.com/journals/jama/fullarticle/2789648>

**international perspectives**

**title:** Covid-19: Ukraine conflict calls Russia’s vaccine diplomacy into question

BMJ| 9th march 2022

Russia’s invasion of Ukraine has marked a new chapter in the saga of Sputnik V—a vaccine intertwined with geopolitics, reports Serena Tinari

Although Russian covid vaccines are licensed in over 70 countries, their success on the international market could be impeded by the conflict in Ukraine and the onset of global sanctions against Russia and its entities.

Sputnik V, a vaccine created by scientists at the Gamaleya National Center of Epidemiology and Microbiology, was developed, promoted, and financed by the Russian Direct Investment Fund (RDIF). On 28 February the US Department of the Treasury included the RDIF in its list of sanctioned Russian entities,1 and the Council of Europe and several national executives worldwide promptly followed…
<https://www.bmj.com/content/376/bmj.o626>

**title:** Pandemic panic and indiscriminate prescriptions drive India’s antimicrobial resistance

BMJ | 8th march 2022

 Indiscriminate prescriptions during the pandemic are accelerating the crisis of antimicrobial resistance in a country that already had the world’s largest consumption of antibiotics, reports Kamala Thiagarajan
<https://www.bmj.com/content/376/bmj.o596>

**title:** Covid-19: Florida surgeon general says state will be first not to recommend vaccination for children

BMJ | 9th march 2022

A doctor who appeared in a video tweeted by Donald Trump questioning the need for covid lockdowns and promoting the use of unproven treatments has said, in his new post as Florida surgeon general, that the state will recommend against covid vaccination for healthy children. The move goes against the advice of the US Centers for Disease Control and Prevention (CDC)…
<https://www.bmj.com/content/376/bmj.o622>

**title:** Vaccine Misinformation and the First Amendment—The Price of Free Speech

jama | 10tH MARCH 2022

Vaccine misinformation during the COVID-19 pandemic underscores how reverence for freedom of speech in the US intensifies our vulnerability to public health threats. Given what we know about how vaccine misinformation influences vaccine acceptance and how intractable false beliefs are, this misinformation may be among the most significant barriers to controlling infectious disease in the 21st century.
<https://jamanetwork.com/journals/jama-health-forum/fullarticle/2790169>

W[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.

We also produce a range of subject-specific news feeds to ensure our clinical and professional teams stay up to date with developments in their work areas. Please visit our [website](http://www.trftlibraryknowledge.com/) for more information

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