COVID-19 weekly update

21st March 2022

**clinical management**

**title:** Awake prone positioning for non-intubated patients with COVID-19-related acute hypoxaemic respiratory failure: a systematic review and meta-analysis  
  
the lancet respiratory medicine| 16th march 2022  
  
Background: Awake prone positioning has been broadly utilised for non-intubated patients with COVID-19-related acute hypoxaemic respiratory failure, but the results from published randomised controlled trials (RCTs) in the past year are contradictory. We aimed to systematically synthesise the outcomes associated with awake prone positioning, and evaluate these outcomes in relevant subpopulations.

Methods: In this systematic review and meta-analysis, two independent groups of researchers searched MEDLINE, Embase, PubMed, Web of Science, Scopus, MedRxiv, BioRxiv, and ClinicalTrials.gov for RCTs and observational studies (with a control group) of awake prone positioning in patients with COVID-19-related acute hypoxaemic respiratory failure published in English from Jan 1, 2020, to Nov 8, 2021. We excluded trials that included patients intubated before or at enrolment, paediatric patients (ie, younger than 18 years), or trials that did not include the supine position in the control group. The same two independent groups screened studies, extracted the summary data from published reports, and assessed the risk of bias. We used a random-effects meta-analysis to pool individual studies. We used the Grading of Recommendations Assessment, Development, and Evaluation approach to assess the certainty and quality of the evidence. The primary outcome was the reported cumulative intubation risk across RCTs, and effect estimates were calculated as risk ratios (RR;95% CI). The analysis was primarily conducted on RCTs, and observational studies were used for sensitivity analyses. No serious adverse events associated with awake prone positioning were reported. The study protocol was prospectively registered with PROSPERO, CRD42021271285.

Findings: A total of 1243 studies were identified, we assessed 138 full-text articles and received the aggregated results of three unpublished RCTs; therefore, after exclusions, 29 studies were included in the study. Ten were RCTs (1985 patients) and 19 were observational studies (2669 patients). In ten RCTs, awake prone positioning compared with the supine position significantly reduced the need for intubation in the overall population (RR 0·84 [95% CI 0·72–0·97]). A reduced need for intubation was shown among patients who received advanced respiratory support (ie, high-flow nasal cannula or non-invasive ventilation) at enrolment (RR 0·83 [0·71–0·97]) and in intensive care unit (ICU) settings (RR 0·83 [0·71–0·97]) but not in patients receiving conventional oxygen therapy (RR 0·87 [0·45–1·69]) or in non-ICU settings (RR 0·88 [0·44–1·76]). No obvious risk of bias and publication bias was found among the included RCTs for the primary outcome.

Interpretation: In patients with COVID-19-related acute hypoxaemic respiratory failure, awake prone positioning reduced the need for intubation, particularly among those requiring advanced respiratory support and those in ICU settings. Awake prone positioning should be used in patients who have acute hypoxaemic respiratory failure due to COVID-19 and require advanced respiratory support or are treated in the ICU.  
<https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00043-1/fulltext>

**Title:** Effect of Sotrovimab on Hospitalization or Death Among High-risk Patients With Mild to Moderate COVID-19: A Randomized Clinical Trial  
  
JAMA |14th march 2022  
  
Question: Among patients at risk of disease progression, does early treatment of mild to moderate COVID-19 with the neutralizing antibody sotrovimab prevent progression to severe disease?  
  
Findings: In this randomized clinical trial of 1057 participants, treatment with a single intravenous dose of sotrovimab, compared with placebo, resulted in a statistically significant reduction in the proportion of patients who experienced a composite outcome of all-cause hospitalization lasting longer than 24 hours or death through day 29 (1% vs 6%, respectively; adjusted relative risk, 0.21).   
  
Meaning: Findings support sotrovimab as a treatment option for nonhospitalized, high-risk patients with mild to moderate COVID-19, although efficacy against SARS-CoV-2 variants that have emerged since the study was completed is unknown.  
<https://jamanetwork.com/journals/jama/fullarticle/2790246>

**Title:** Efficacy of Losartan in Hospitalized Patients With COVID-19–Induced Lung Injury: A Randomized Clinical Trial  
  
JAMA | 16th march 2022   
  
Question: What is the effect of losartan on lung injury in hospitalized patients with COVID-19?

Findings: In this randomized clinical trial in 205 patients with evidence of COVID-19–induced acute lung injury, angiotensin receptor blockade with maximal dose losartan did not reduce lung injury at 7 days, as measured by partial pressure of oxygen to fraction of inspired oxygen ratio. Secondary outcomes, including ventilator-free days and mortality, were unaffected, but patients treated with losartan had fewer vasopressor-free days.

Meaning: This randomized clinical trial found that losartan for angiotensin receptor blockade did not reduce lung injury in patients with COVID-19 and raised concerns about risks of harm.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790162>

**Title:** The Fragility of Statistically Significant Results in Randomized Clinical Trials for COVID-19  
  
JAMA| 18th march 2022  
  
Question: In randomized clinical trials (RCTs) of COVID-19 that report statistically significant results, what is the fragility index, ie, the minimum number of participants who would need to have had a different outcome for the RCT to lose statistical significance?

Findings: In this cross-sectional study of 47 RCTs with a total of 138 235 participants that had statistically significant results, the median fragility index was 4. That is, a median of 4 events was required to change the analysis findings from statistically significant to not significant.

Meaning: In this study, many RCTs for COVID-19 had a low fragility index, challenging confidence in the robustness of the results.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790259>

**covid rates & variants**

**title:** Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 omicron (B.1.1.529) and delta (B.1.617.2) variants in England: a cohort study  
  
the lancet | 16th mARCH 2022

Background: The omicron variant (B.1.1.529) of SARS-CoV-2 has demonstrated partial vaccine escape and high transmissibility, with early studies indicating lower severity of infection than that of the delta variant (B.1.617.2). We aimed to better characterise omicron severity relative to delta by assessing the relative risk of hospital attendance, hospital admission, or death in a large national cohort.

Methods: Individual-level data on laboratory-confirmed COVID-19 cases resident in England between Nov 29, 2021, and Jan 9, 2022, were linked to routine datasets on vaccination status, hospital attendance and admission, and mortality. The relative risk of hospital attendance or admission within 14 days, or death within 28 days after confirmed infection, was estimated using proportional hazards regression. Analyses were stratified by test date, 10-year age band, ethnicity, residential region, and vaccination status, and were further adjusted for sex, index of multiple deprivation decile, evidence of a previous infection, and year of age within each age band. A secondary analysis estimated variant-specific and vaccine-specific vaccine effectiveness and the intrinsic relative severity of omicron infection compared with delta (ie, the relative risk in unvaccinated cases).

Findings: The adjusted hazard ratio (HR) of hospital attendance (not necessarily resulting in admission) with omicron compared with delta was 0·56 (95% CI 0·54–0·58); for hospital admission and death, HR estimates were 0·41 (0·39–0·43) and 0·31 (0·26–0·37), respectively. Omicron versus delta HR estimates varied with age for all endpoints examined. The adjusted HR for hospital admission was 1·10 (0·85–1·42) in those younger than 10 years, decreasing to 0·25 (0·21–0·30) in 60–69-year-olds, and then increasing to 0·47 (0·40–0·56) in those aged at least 80 years. For both variants, past infection gave some protection against death both in vaccinated (HR 0·47 [0·32–0·68]) and unvaccinated (0·18 [0·06–0·57]) cases. In vaccinated cases, past infection offered no additional protection against hospital admission beyond that provided by vaccination (HR 0·96 [0·88–1·04]); however, for unvaccinated cases, past infection gave moderate protection (HR 0·55 [0·48–0·63]). Omicron versus delta HR estimates were lower for hospital admission (0·30 [0·28–0·32]) in unvaccinated cases than the corresponding HR estimated for all cases in the primary analysis. Booster vaccination with an mRNA vaccine was highly protective against hospitalisation and death in omicron cases (HR for hospital admission 8–11 weeks post-booster vs unvaccinated: 0·22 [0·20–0·24]), with the protection afforded after a booster not being affected by the vaccine used for doses 1 and 2.

Interpretation: The risk of severe outcomes following SARS-CoV-2 infection is substantially lower for omicron than for delta, with higher reductions for more severe endpoints and significant variation with age. Underlying the observed risks is a larger reduction in intrinsic severity (in unvaccinated individuals) counterbalanced by a reduction in vaccine effectiveness. Documented previous SARS-CoV-2 infection offered some protection against hospitalisation and high protection against death in unvaccinated individuals, but only offered additional protection in vaccinated individuals for the death endpoint. Booster vaccination with mRNA vaccines maintains over 70% protection against hospitalisation and death in breakthrough confirmed omicron infections.  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00462-7/fulltext>

**title:** Omicron: fewer adverse outcomes come with new dangers  
  
JAMA | 18th mARCH 2022  
  
With wave after wave of SARS-CoV-2 variants, COVID-19 patients filled the worlds' hospitals and morgues because not everybody had access to vaccines or were willing to be vaccinated. Omicron (B.1.1.529) is no different. Although most scientists were expecting an increase in cases during late 2021, it was surprising that vaccinated and previously infected people were contracting the novel omicron variant so easily and how fast it was transmitting, which raised several questions. Would existing vaccines still prevent SARS-CoV-2 infection? Was omicron more transmissible than previous variants? What were the consequences of omicron's wide and rapid spread infecting millions of people, including a high number of breakthrough cases? Would it have worse or better outcomes than the worst SARS-CoV-2 variant on record, the delta variant (B.1.617.2)? In The Lancet, Tommy Nyberg and colleagues report their findings about omicron for individuals who are vaccinated, previously infected, or unvaccinated. This outstanding study included an unparalleled 37% of SARS-CoV-2 cases in England. A longitudinal cohort was analysed when the delta variant was still ongoing and omicron outcompeted delta to become the dominant variant…  
  
… Although this study is timely and an important contribution to the SARS-CoV-2 literature, there are also some limitations. Despite decreased individual risks for hospitalisation and death (omicron vs delta), Nyberg and colleagues did not emphasise the considerable threat to public health. Given that omicron is more transmissible than the delta variant, there were record levels of cases globally that led to record numbers of hospitalisations in some countries, such as the USA. For every new infection, there is the risk of SARS-CoV-2 evolving yet again due to novel mutations, either within the omicron lineages (such as further evolution of the BA.1 and BA.2 omicron subvariants) or from new independent lineages (as has happened with every variant of concern thus far). However, as this study shows, omicron has led to a new pandemic scenario where a substantial proportion of the population in countries with high incidence rates has acquired immunity either through vaccination, infection, or both. In this environment, spikes in hospitalisations are rarer due to a combination of pre-existing immunity and selection of less pathogenic SARS-CoV-2 variants, such as omicron. Yet, we cannot dismiss the fact that highly pathogenic or transmissible variants might develop. In low-income and middle-income countries where fewer people are vaccinated, SARS-CoV-2 will diversify more rapidly.

The global community must keep pushing for equity in access to COVID-19 vaccines and treatments in countries with low immunisation rates. Preventing the spread of SARS-CoV-2 will obstruct the virus from adapting whilst more directed data-driven prevention measures are implemented in highly immunised countries. With advancing SARS-CoV-2 knowledge—especially from large studies like that of Nyberg and colleagues—together with new and developing vaccines, treatments, and therapeutics, we might be on the precipice of more targeted, preventive measures that allow us to avoid blanket, highly restrictive policies that have harmful costs to the economy, society, and public health.  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00514-1/fulltext>

**title:** Age-Varying Susceptibility to the Delta Variant (B.1.617.2) of SARS-CoV-2  
  
JAMA | 18th mARCH 2022  
  
Question: Is the Delta variant (B.1.617.2) more transmissible than previous strains of SARS-CoV-2 among children and adolescents?

Findings: This decision analytic model of 106 866 confirmed COVID-19 infections found that the increase in susceptibility to the Delta vs pre-Delta variant was highest in the group aged 10 to 15 years, with an increase of 1.92-fold.

Meaning: This study found that even after adjusting for contact pattern and vaccination status, the Delta variant of SARS-CoV-2 was estimated to propagate more easily among children than pre-Delta strains.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790253>

**title:** Covid-19: Is the UK heading for another omicron wave?  
  
bmj | 18th mARCH 2022  
  
With covid cases and hospital admissions again rising, Elisabeth Mahase examines what is driving the trend.

After several weeks of decline, global covid-19 case numbers are rising again. Parts of Asia such as Hong Kong are experiencing huge and deadly surges of the virus. In the UK, cases and hospital admissions, which had been falling since the omicron peak in January, are now increasing. The latest figures from NHS Test and Trace show that in England a total of 323 032 people tested positive for SARS-CoV-2 between 3 and 9 March 2022, an increase of 55.5% from the previous week. The Office for National Statistics, which collects its own separate data, has reported that in the week ending 12 March around 1 in 20 people in England were infected with the virus—up from one in 25 the week before. In Wales an estimated one in 25 people had covid-19 during that week, up from 1 in 30 people the week before. In Northern Ireland there was a slight decrease from one in 13 the week before to one in 14, and in Scotland the rate rose from one in 18 to one in 14. Latest data from NHS England show a similar trend with hospital admissions. While daily covid-19 admissions had been declining—from a peak of 2317 on 29 December 2021, down to 786 on 25 February 2022—they have now started to rise again. Since 28 February daily admissions to hospitals in England have been almost consistently above 1000, and on 13 March the number hit 1555…  
<https://www.bmj.com/content/376/bmj.o738>

**title:** Monitoring and managing SARS-CoV-2 evolution in immunocompromised populations  
  
the lancet microbe | 15th mARCH 2022  
  
Since the start of the COVID-19 pandemic in late 2019, five SARS-CoV-2 variants of concern have emerged. The omicron (B.1.1.529) variant, first identified in November, 2021, has more than 20 vital mutations in the spike protein alone, and has rapidly spread across the world within 2 months. We hypothesise that SARS-CoV-2 infection in immunocompromised populations might propagate SARS-CoV-2 evolution and accelerate the emergence of variants .

<https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(22)00061-1/fulltext>

**long-term effects:**

**title:** Are we mislabelling long covid in children and adolescents? [Letter]  
  
BMJ | 18th mARCH 2022  
  
…By uncritically applying a label of long covid, we risk mislabelling patients with mental health problems and, even worse, perpetuating and strengthening symptoms in people predisposed to such problems. Describing new medical conditions and labelling patients should not be considered without risks.  
<https://www.bmj.com/content/376/bmj.o705.full>

**infection control**

**title:** SARS-CoV-2 positivity in offspring and timing of mother-to-child transmission

BMJ |16th march 2022  
  
Objectives To assess the rates of SARS-CoV-2 positivity in babies born to mothers with SARS-CoV-2 infection, the timing of mother-to-child transmission and perinatal outcomes, and factors associated with SARS-CoV-2 status in offspring. Design Living systematic review and meta-analysis. Data sources Major databases between 1 December 2019 and 3 August 2021. Study selection Cohort studies of pregnant and recently pregnant women (including after abortion or miscarriage) who sought hospital care for any reason and had a diagnosis of SARS-CoV-2 infection, and also provided data on offspring SARS-CoV-2 status and risk factors for positivity. Case series and case reports were also included to assess the timing and likelihood of mother-to-child transmission in SARS-CoV-2 positive babies. Data extraction Two reviewers independently extracted data and assessed study quality. A random effects model was used to synthesise data for rates, with associations reported using odds ratios and 95% confidence intervals. Narrative syntheses were performed when meta-analysis was inappropriate. The World Health Organization classification was used to categorise the timing of mother-to-child transmission (in utero, intrapartum, early postnatal).

Results: 472 studies (206 cohort studies, 266 case series and case reports; 28 952 mothers, 18 237 babies) were included. Overall, 1.8% (95% confidence interval 1.2% to 2.5%; 140 studies) of the 14 271 babies born to mothers with SARS-CoV-2 infection tested positive for the virus with reverse transcriptase polymerase chain reaction (RT-PCR). Of the 592 SARS-CoV-2 positive babies with data on the timing of exposure and type and timing of tests, 14 had confirmed mother-to-child transmission: seven in utero (448 assessed), two intrapartum (18 assessed), and five during the early postnatal period (70 assessed). Of the 800 SARS-CoV-2 positive babies with outcome data, 20 were stillbirths, 23 were neonatal deaths, and eight were early pregnancy losses; 749 babies were alive at the end of follow-up. Severe maternal covid-19 (odds ratio 2.4, 95% confidence interval 1.3 to 4.4), maternal death (14.1, 4.1 to 48.0), maternal admission to an intensive care unit (3.5, 1.7 to 6.9), and maternal postnatal infection (5.0, 1.2 to 20.1) were associated with SARS-CoV-2 positivity in offspring. Positivity rates using RT-PCR varied between regions, ranging from 0.1% (95% confidence interval 0.0% to 0.3%) in studies from North America to 5.7% (3.2% to 8.7%) in studies from Latin America and the Caribbean.

Conclusion: SARS-CoV-2 positivity rates were found to be low in babies born to mothers with SARS-CoV-2 infection. Evidence suggests confirmed vertical transmission of SARS-CoV-2, although this is likely to be rare. Severity of maternal covid-19 appears to be associated with SARS-CoV-2 positivity in offspring.  
<https://www.bmj.com/content/376/bmj-2021-067696>

**title:** Transmission of SARS-CoV-2 from mother to baby is rare

BMJ| 16th march 2022  
  
Despite hundreds of millions of confirmed SARS-CoV-2 infections and more than five million related deaths worldwide major gaps remain in our knowledge about the risks to babies when their mothers are infected with SARS-CoV-2. Allotey and colleagues (doi:[10.1136/bmj-2021-067696](https://www.bmj.com/lookup/doi/10.1136/bmj-2021-067696)), in their work for the PregCOV-19 Living Systematic Review Consortium, help address this gap with a review of nearly 500 studies. Their study provides vital information on mother-to-child transmission of SARS-CoV-2, including rates of positivity among babies born to mothers with the virus, the likely timing of mother-to-child transmission, clinical outcomes among babies with the virus, and whether maternal characteristics or factors associated with labour, delivery, or breastfeeding increase the risk of babies becoming infected…  
  
…Although some important conclusions can be drawn from this review, the paucity of high quality data on risks to infants from covid-19 is also highlighted. Despite hundreds of millions of infections and a review of nearly 500 studies from across the globe, sufficient data were only available for 14 518 exposed babies worldwide to determine positivity rates, with large variability in the numbers of studies, events, and total exposed cases by world region. Furthermore, data to determine outcomes, such as death, were available from only 800 babies positive for SARS-CoV-2. Sufficient data to ascertain the timing of exposure and likelihood of infection among exposed babies were only available for 592 babies. Given that vaccines are not available for babies and young children, it is critical that better data become available to inform appropriate shared decision making on perinatal care between parents and healthcare providers.  
<https://www.bmj.com/content/376/bmj.o593>

**title:** Association between covid-19 vaccination, SARS-CoV-2 infection, and risk of immune mediated neurological events

bmj | 16th march 2022  
  
Objective To study the association between covid-19 vaccines, SARS-CoV-2 infection, and risk of immune mediated neurological events. Design Population based historical rate comparison study and self-controlled case series analysis. Setting Primary care records from the United Kingdom, and primary care records from Spain linked to hospital data. Participants 8 330 497 people who received at least one dose of covid-19 vaccines ChAdOx1 nCoV-19, BNT162b2, mRNA-1273, or Ad.26.COV2.S between the rollout of the vaccination campaigns and end of data availability (UK: 9 May 2021; Spain: 30 June 2021). The study sample also comprised a cohort of 735 870 unvaccinated individuals with a first positive reverse transcription polymerase chain reaction test result for SARS-CoV-2 from 1 September 2020, and 14 330 080 participants from the general population.

Main outcome measures Outcomes were incidence of Bell’s palsy, encephalomyelitis, Guillain-Barré syndrome, and transverse myelitis. Incidence rates were estimated in the 21 days after the first vaccine dose, 90 days after a positive test result for SARS-CoV-2, and between 2017 and 2019 for background rates in the general population cohort. Indirectly standardised incidence ratios were estimated. Adjusted incidence rate ratios were estimated from the self-controlled case series.

Results The study included 4 376 535 people who received ChAdOx1 nCoV-19, 3 588 318 who received BNT162b2, 244 913 who received mRNA-1273, and 120 731 who received Ad26.CoV.2; 735 870 people with SARS-CoV-2 infection; and 14 330 080 people from the general population. Overall, post-vaccine rates were consistent with expected (background) rates for Bell’s palsy, encephalomyelitis, and Guillain-Barré syndrome. Self-controlled case series was conducted only for Bell’s palsy, given limited statistical power, but with no safety signal seen for those vaccinated. Rates were, however, higher than expected after SARS-CoV-2 infection. For example, in the data from the UK, the standardised incidence ratio for Bell’s palsy was 1.33 (1.02 to 1.74), for encephalomyelitis was 6.89 (3.82 to 12.44), and for Guillain-Barré syndrome was 3.53 (1.83 to 6.77). Transverse myelitis was rare (<5 events in all vaccinated cohorts) and could not be analysed.

Conclusions No safety signal was observed between covid-19 vaccines and the immune mediated neurological events of Bell’s palsy, encephalomyelitis, Guillain-Barré syndrome, and transverse myelitis. An increased risk of Bell’s palsy, encephalomyelitis, and Guillain-Barré syndrome was, however, observed for people with SARS-CoV-2 infection.  
<https://www.bmj.com/content/376/bmj-2021-068373>

**title:** The neurological safety of covid-19 vaccines [editorial]  
  
bmj| 16th march 2022

Real world evidence is broadly reassuring

Leveraging data on 8.3 million people from two large electronic health record databases in the UK and Spain, Li and colleagues (doi:10.1136/bmj-2021-068373) studied the association between covid-19 vaccines, either vector based or mRNA, and immune mediated neurological outcomes.1 Neither the ChAdOx1 nCoV-19 (Oxford-AstraZeneca) nor the BNT162b2 (Pfizer-BioNTech) vaccine was associated with an increased risk of neurological adverse events. Conversely, increased risks of all studied neurological outcomes were seen after SARS-CoV-2 infection. However, the power to detect small or even moderate increases in rare neurological outcomes—such as Bell’s palsy, encephalomyelitis, Guillain-Barré syndrome, and transverse myelitis—after vaccination was limited, despite the relatively large study population. Another key limitation acknowledged by the authors was lack of adjustment for patient characteristics other than age in the majority of the analyses. This might have led to overestimation of risks associated with SARS-CoV-2 infection, as patients with the infection had more comorbidity than the background population…  
<https://www.bmj.com/content/376/bmj.o522>

**title:** Myocarditis Following a Third BNT162b2 Vaccination Dose in Military Recruits in Israel

JAMA| 17th march 2022  
  
Vaccination has limited SARS-CoV-2 spread and prevented major illness and death during the COVID-19 pandemic. However, certain adverse events, such as an increased incidence of myocarditis, particularly in young men, have been associated with vaccination with the BNT162b2 mRNA vaccine (Pfizer-BioNTech). On July 30, 2021, the Israeli Ministry of Health approved the administration of a third vaccine dose for the general population in response to increasing numbers of COVID-19 cases. We assessed whether a third vaccine dose was associated with the risk of myocarditis…  
  
…This study found a low risk of myocarditis after a third dose of BNT162b2 in Israeli military recruits. The incidence was lower than observed a week after a second dose of the vaccine in a similar Israeli military population (5.07 per 100 000 vaccines).4 However, the myocarditis incidence for 18- to 24-year-old men was higher than observed for a US male population (5.243 per 100 000 vaccines).3 The incidence of myocarditis following the second dose of the vaccine varies according to follow-up times in studies2-6 and the definition of myocarditis used. Therefore, comparisons should be made with caution.

Study limitations included the small number of diagnosed cases and inclusion primarily of young men. However, the study included the entire IDF vaccinated population, which is representative of the IDF population in age and sex distribution. Because the study included only cases diagnosed in the hospital, there is a chance for underdiagnosis, and the incidence of myocarditis may be higher. However, the risk of underascertainment is likely low because awareness of postvaccination myocarditis was high as a result of media coverage and because all suspected myocarditis cases were referred for hospital assessment.

The cause of the lower incidence of myocarditis following a third dose in comparison with the incidence after the second dose requires future research.  
<https://jamanetwork.com/journals/jama/fullarticle/2790421>

**title:** INCIDENCE OF CEREBRAL VENOUS THROMBOSIS FOLLOWING SARS-COV-2 INFECTION VS MRNA SARS-COV-2 VACCINATION IN SINGAPORE

jama | 17th march 2022  
  
Question What is the risk of cerebral venous thrombosis (CVT) after diagnosis of SARS-CoV-2 infection compared with after messenger RNA (mRNA)-based SARS-CoV-2 vaccination?

Findings In this observational cohort study of 62 447 individuals with SARS-CoV-2 infection and 3 006 662 individuals who received mRNA-based SARS-CoV-2 vaccine in Singapore from January 23, 2020, to August 3, 2021, the incidence rate ratio of CVT requiring hospitalization within 6 weeks of SARS-CoV-2 infection was 32 times higher compared with after mRNA-based SARS-CoV-2 vaccination.

Meaning These findings suggest that the risk of CVT after SARS-CoV-2 infection is higher than after mRNA-based SARS-CoV-2 vaccination.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790206>

**title:** Comparative Effectiveness of Single vs Repeated Rapid SARS-CoV-2 Antigen Testing Among Asymptomatic Individuals in a Workplace Setting

jama| 18th march 2022  
  
…The results of this study demonstrated that when a repeated rapid antigen test was offered to participants of an employee screening program, the estimated accuracy increased from 38% to 92% for true-positive results as determined by RT-qPCR for SARS-CoV-2. These findings may have important implications for how rapid antigen tests can be deployed for more accurate results,5,6 especially in a setting where the time to results is important and where widespread PCR testing may be cost prohibitive.

Limitations of the study were that all employees were asymptomatic and were screened as part of a workplace testing program. As expected, test results appeared to be more accurate when community infection rates were higher and, therefore, the pretest probability was higher. The diagnostic value of a second antigen test remained high regardless of pretest probability. As employers consider the best use of onsite or at-home rapid antigen testing, a second antigen test may be useful for more accurate diagnosis of COVID-19 infection and for guiding intervention.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790263>

**title:** Covid-19: Updated PPE guidance puts NHS staff at risk of infection, say medics

BMJ| 18th march 2022  
  
NHS staff face unacceptable health risks as a result of “retrograde” changes to the government’s guidance on preventing spread of SARS-CoV-2 infection, doctors’ leaders have warned.

The BMA said on 16 March it was concerned over updated guidance issued by the UK Health Security Agency covering use of personal protective equipment.1 It said the guidance failed to properly acknowledge that SARS-CoV-2 infection can spread in the air during the routine care of patients as they cough or sneeze and not just when specific processes known as aerosol generating procedures (AGPs) are being undertaken.

“This is a retrograde step as it once again means that healthcare workers will not be routinely provided the right level of protective masks and equipment they need to be safe at work when looking after covid patients,” said Chaand Nagpaul, the BMA’s chair of council.

The BMA said it was crucial that any staff looking after patients with confirmed or suspected covid-19, or in other situations where a local risk assessment required it, had access to respiratory protective equipment such as filtering face piece (FFP3) masks…  
<https://www.bmj.com/content/376/bmj.o733>

**title:** Covid-19: Evusheld is approved in UK for prophylaxis in immunocompromised people  
  
BMJ| 17th march 2022  
  
The UK’s drug regulator has approved a combination of two monoclonal antibodies to prevent covid-19 in people who are unlikely to mount an immune response from vaccination or for whom vaccination is not recommended.

Evusheld, a combination of the two long acting antibodies tixagevimab and cilgavimab, is authorised for covid-19 prevention by the Medicines and Healthcare Products Regulatory Agency (MHRA). The government’s independent advisory body, the Commission on Human Medicines, endorsed the approval after independently reviewing the evidence…  
<https://www.bmj.com/content/376/bmj.o722>

**title:** Covid-19: Pfizer asks US regulator to authorise fourth vaccine dose for over 65s

BMJ| 17th march 2022  
  
Pfizer and BioNTech have applied to the US Food and Drug Administration for emergency use authorisation for a fourth dose of its mRNA vaccine against covid-19 for adults aged 65 and older. The companies said that the additional dose reduced the rates of infection and severe illness in older adults. In a press release they said that they were seeking the new approval for adults over 65 who had received an initial booster of any of the authorised or approved covid-19 vaccines..  
<https://www.bmj.com/content/376/bmj.o711>

**title:** Effectiveness of rAd26-rAd5, ChAdOx1 nCoV-19, and BBIBP-CorV vaccines for risk of infection with SARS-CoV-2 and death due to COVID-19 in people older than 60 years in Argentina: a test-negative, case-control, and retrospective longitudinal study

the lancet| 15th march 2022  
  
Background: In January, 2021, a vaccination campaign against COVID-19 was initiated with the rAd26-rAd5, ChAdOx1 nCoV-19, and BBIBP-CorV vaccines in Argentina. The objective of this study was to estimate vaccine effectiveness at reducing risk of SARS-CoV-2 infection and COVID-19 deaths in people older than 60 years.

Methods: In this test-negative, case-control, and retrospective longitudinal study done in Argentina, we evaluated the effectiveness of three vaccines (rAd26-rAd5, ChAdOx1 nCoV-19, and BBIBP-CorV) on SARS-CoV-2 infection and risk of death in people with RT-PCR confirmed COVID-19, using data from the National Surveillance System (SNVS 2.0). All individuals aged 60 years or older reported to SNVS 2.0 as being suspected to have COVID-19 who had disease status confirmed with RT-PCR were included in the study. Unvaccinated individuals could participate in any of the analyses. People with suspected COVID-19 who developed symptoms before the start of the implementation of the vaccination programme for their age group or district were excluded from the study. The odds ratio of SARS-CoV-2 infection was evaluated by logistic regression and the risk of death in individuals with RT-PCR confirmed COVID-19 was evaluated by proportional hazard regression models, adjusted for possible confounders: age at the time of the symptom onset date, sex, district of residence, epidemiological week corresponding to the symptom onset date, and history of COVID-19. The estimation of vaccine effectiveness to prevent death due to COVID-19 was done indirectly by combining infection and death estimates. In addition, we evaluated the effect of the first dose of viral vector vaccines across time.

Findings: From Jan 31, to Sept 14, 2021, 1 282 928 individuals were included, of whom 687 167 (53·6%) were in the rAd26-rAd5 analysis, 358 431 (27·6%) in the ChAdOx1 nCoV-19 analysis, and 237 330 (18·5%) in the BBIBP-CorV analysis. Vaccine effectiveness after two doses was high for all three vaccines, adjusted odds ratio 0·36 (95% CI 0·35–0·37) for rAd26-rAd5, 0·32 (0·31–0·33) for ChAdOx1 nCoV-19, and 0·56 (0·55–0·58) for BBIBP-CorV. After two doses, the effect on deaths was higher than that on risk of infection: adjusted hazard ratio 0·19 (95% CI 0·18–0·21) for rAd26-rAd5, 0·20 (0·18–0·22) for ChAdOx1 nCoV-19, and 0·27 (0·25–0·29) for BBIBP-CorV. The indirectly estimated effectiveness on deaths was 93·1% (95% CI 92·6–93·5) for rAd26-rAd5, 93·7% (93·2–94·3) for ChAdOx1 nCoV-19, and 85·0% (84·0–86·0) for BBIBP-CorV following two doses. First dose effect of viral vector vaccines remained stable over time.

Interpretation: The vaccines used in Argentina showed effectiveness in reducing infection and death by SARS-CoV-2 and COVID-19  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00011-3/fulltext>

**title:** Evaluating COVID-19 vaccines in the real world

the lancet| 15th march 2022

…The many questions answered by Rearte and colleagues are important to every country that is choosing which vaccines to distribute. Evidence that the rAd26-rAd5 and ChAdOx1 nCoV-19 vaccines offer slightly more protection than BBIBP-CorV should be balanced with the costs and availability of these vaccines. An important factor to consider is emerging evidence that indicates mixing vaccines offers favourable outcomes and supports distribution of any vaccine that is readily available.  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00194-5/fulltext>

**title:** Efficacy of a Fourth Dose of Covid-19 mRNA Vaccine against Omicron

new england journal of medicine | 16th march 2022  
  
… Our data provide evidence that a fourth dose of mRNA vaccine is immunogenic, safe, and somewhat efficacious (primarily against symptomatic disease). A comparison of the initial response to the fourth dose with the peak response to a third dose did not show substantial differences in humoral response or in levels of omicron-specific neutralizing antibodies. Along with previous data showing the superiority of a third dose to a second dose our results suggest that maximal immunogenicity of mRNA vaccines is achieved after three doses and that antibody levels can be restored by a fourth dose. Furthermore, we observed low vaccine efficacy against infections in health care workers, as well as relatively high viral loads suggesting that those who were infected were infectious. Thus, a fourth vaccination of healthy young health care workers may have only marginal benefits. Older and vulnerable populations were not assessed.  
<https://www.nejm.org/doi/full/10.1056/NEJMc2202542?query=featured_coronavirus>

**title:** Neutralization of the SARS-CoV-2 Omicron BA.1 and BA.2 Variants

new england journal of medicine| 16th march 2022  
  
…Overall, these data show that neutralizing antibody titers against BA.2 were similar to those against BA.1, with median titers against BA.2 that were lower than those against BA.1 by a factor of 1.3 to 1.4. A third dose of the BNT162b2 vaccine was needed for induction of consistent neutralizing antibody titers against either BA.1 or BA.2.3,4 Moreover, in vaccinated persons who had presumably been infected with BA.1, robust neutralizing antibody titers against BA.2 developed, which suggests a substantial degree of cross-reactive natural immunity. These findings have important public health implications and suggest that the increasing frequency of BA.2 in the context of the BA.1 surge is probably related to increased transmissibility rather than to enhanced immunologic escape.  
<https://www.nejm.org/doi/full/10.1056/NEJMc2201849?query=featured_coronavirus>

**title:** Effectiveness of the Ad26.COV2.S vaccine in health-care workers in South Africa (the Sisonke study): results from a single-arm, open-label, phase 3B, implementation study

the lancet| 19th march 2022  
  
Background: We aimed to assess the effectiveness of a single dose of the Ad26.COV2.S vaccine (Johnson & Johnson) in health-care workers in South Africa during two waves of the South African COVID-19 epidemic.

Methods: In the single-arm, open-label, phase 3B implementation Sisonke study, health-care workers aged 18 years and older were invited for vaccination at one of 122 vaccination sites nationally. Participants received a single dose of 5 × 1010 viral particles of the Ad26.COV2.S vaccine. Vaccinated participants were linked with their person-level data from one of two national medical insurance schemes (scheme A and scheme B) and matched for COVID-19 risk with an unvaccinated member of the general population. The primary outcome was vaccine effectiveness against severe COVID-19, defined as COVID-19-related admission to hospital, hospitalisation requiring critical or intensive care, or death, in health-care workers compared with the general population, ascertained 28 days or more after vaccination or matching, up to data cutoff. This study is registered with the South African National Clinical Trial Registry, DOH-27-022021-6844, ClinicalTrials.gov, NCT04838795, and the Pan African Clinical Trials Registry, PACTR202102855526180, and is closed to accrual.

Findings: Between Feb 17 and May 17, 2021, 477 102 health-care workers were enrolled and vaccinated, of whom 357 401 (74·9%) were female and 119 701 (25·1%) were male, with a median age of 42·0 years (33·0–51·0). 215 813 vaccinated individuals were matched with 215 813 unvaccinated individuals. As of data cutoff (July 17, 2021), vaccine effectiveness derived from the total matched cohort was 83% (95% CI 75–89) to prevent COVID-19-related deaths, 75% (69–82) to prevent COVID-19-related hospital admissions requiring critical or intensive care, and 67% (62–71) to prevent COVID-19-related hospitalisations. The vaccine effectiveness for all three outcomes were consistent across scheme A and scheme B. The vaccine effectiveness was maintained in older health-care workers and those with comorbidities including HIV infection. During the course of the study, the beta (B.1.351) and then the delta (B.1.617.2) SARS-CoV-2 variants of concerns were dominant, and vaccine effectiveness remained consistent (for scheme A plus B vaccine effectiveness against COVID-19-related hospital admission during beta wave was 62% [95% CI 42–76] and during delta wave was 67% [62–71], and vaccine effectiveness against COVID-19-related death during beta wave was 86% [57–100] and during delta wave was 82% [74–89]).

Interpretation: The single-dose Ad26.COV2.S vaccine shows effectiveness against severe COVID-19 disease and COVID-19-related death after vaccination, and against both beta and delta variants, providing real-world evidence for its use globally.  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00007-1/fulltext>

**title:** Neutralisation sensitivity of the SARS-CoV-2 omicron (B.1.1.529) variant: a cross-sectional study

the lancet| 17th march 2022  
  
Background: The SARS-CoV-2 omicron (B.1.1.529) variant, which was first identified in November, 2021, spread rapidly in many countries, with a spike protein highly diverged from previously known variants, and raised concerns that this variant might evade neutralising antibody responses. We therefore aimed to characterise the sensitivity of the omicron variant to neutralisation.

Methods: For this cross-sectional study, we cloned the sequence encoding the omicron spike protein from a diagnostic sample to establish an omicron pseudotyped virus neutralisation assay. We quantified the neutralising antibody ID50 (the reciprocal dilution that produces 50% inhibition) against the omicron spike protein, and the fold-change in ID50 relative to the spike of wild-type SARS-CoV-2 (ie, the pandemic founder variant), for one convalescent reference plasma pool (WHO International Standard for anti-SARS-CoV-2 immunoglobulin [20/136]), three reference serum pools from vaccinated individuals, and two cohorts from Stockholm, Sweden: one comprising previously infected hospital workers (17 sampled in November, 2021, after vaccine rollout and nine in June or July, 2020, before vaccination) and one comprising serum from 40 randomly sampled blood donors donated during week 48 (Nov 29–Dec 5) of 2021. Furthermore, we assessed the neutralisation of omicron by five clinically relevant monoclonal antibodies (mAbs).

Findings: Neutralising antibody responses in reference sample pools sampled shortly after infection or vaccination were substantially less potent against the omicron variant than against wild-type SARS-CoV-2 (seven-fold to 42-fold reduction in ID50 titres). Similarly, for sera obtained before vaccination in 2020 from a cohort of convalescent hospital workers, neutralisation of the omicron variant was low to undetectable (all ID50 titres <20). However, in serum samples obtained in 2021 from two cohorts in Stockholm, substantial cross-neutralisation of the omicron variant was observed. Sera from 17 hospital workers after infection and subsequent vaccination had a reduction in average potency of only five-fold relative to wild-type SARS-CoV-2 (geometric mean ID50 titre 495 vs 105), and two donors had no reduction in potency. A similar pattern was observed in randomly sampled blood donors (n=40), who had an eight-fold reduction in average potency against the omicron variant compared with wild-type SARS-CoV-2 (geometric mean ID50 titre 369 vs 45). We found that the omicron variant was resistant to neutralisation (50% inhibitory concentration [IC50] >10 μg/mL) by mAbs casirivimab (REGN-10933), imdevimab (REGN-10987), etesevimab (Ly-CoV016), and bamlanivimab (Ly-CoV555), which form part of antibody combinations used in the clinic to treat COVID-19. However, S309, the parent of sotrovimab, retained most of its activity, with only an approximately two-fold reduction in potency against the omicron variant compared with ancestral D614G SARS-CoV-2 (IC50 0·1–0·2 μg/mL).

Interpretation: These data highlight the extensive, but incomplete, evasion of neutralising antibody responses by the omicron variant, and suggest that boosting with licensed vaccines might be sufficient to raise neutralising antibody titres to protective levels.  
<https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00129-3/fulltext>

**title:** SARS-CoV-2 incidence, transmission, and reinfection in a rural and an urban setting: results of the PHIRST-C cohort study, South Africa, 2020–21

the lancet infectious diseases| 14th march 2022  
  
By August, 2021, South Africa had been affected by three waves of SARS-CoV-2; the second associated with the beta variant and the third with the delta variant. Data on SARS-CoV-2 burden, transmission, and asymptomatic infections from Africa are scarce. We aimed to evaluate SARS-CoV-2 burden and transmission in one rural and one urban community in South Africa. We conducted a prospective cohort study of households in Agincourt, Mpumalanga province (rural site) and Klerksdorp, North West province (urban site) from July, 2020 to August, 2021. We randomly selected households for the rural site from a health and sociodemographic surveillance system and for the urban site using GPS coordinates. Households with more than two members and where at least 75% of members consented to participate were eligible…

…In this study, 565 (85·3%) SARS-CoV-2 infections were asymptomatic and index case symptom status did not affect HCIR, suggesting a limited role for control measures targeting symptomatic individuals. Increased household transmission of beta and delta variants was likely to have contributed to successive waves of SARS-CoV-2 infection, with more than 60% of individuals infected by the end of follow-up.  
<https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00069-X/fulltext>

**title:** SARS-CoV-2 transmission: time to rethink public health strategy  
  
the lancet infectious diseases | 14th march 2022   
  
The prospective household cohort study of SARS-CoV-2, influenza, and respiratory syncytial virus community burden, transmission dynamics, and viral interaction in South Africa (PHIRST-C) by Cohen and colleagues comprehensively investigated the incidence, reinfection, and transmission dynamics within urban and rural households in South Africa. Novel study methodology included intensive symptom screening, midturbinate nasal swabs twice a week for testing of SARS-CoV-2 with real-time RT-PCR (RT-rtPCR; irrespective of symptoms), and anti-SARS-CoV-2 antibody testing every 2 months. The study period coincided with three COVID-19 waves in South Africa, which were driven by original wild-type variant in the first wave, the beta variant in the second wave, and the delta variant in the third wave.

The study reports that 749 (62·4%) of 1200 participants were infected with SARS-CoV-2, based on RT-rtPCR and serology combined, and 87 (11·6%) of 749 were reinfected. The prevalence of asymptomatic infection was high (565 [85·3%] of 662 RT-rtPCR-confirmed episodes with available data), even in older participants (≥19 years; 220 [76·1%] of 289), when compared with a previous systematic review of 79 studies (1287 [19·5%] of 6616).

In contrast to existing evidence, this study showed that household cumulative infection rate (transmissibility from the index case to susceptible household members) was similar between asymptomatic index cases (23·9% [175 of 731 susceptible household members infected]) and symptomatic index cases (23·3% [20 of 86]; odds ratio [OR] 1·0 [95% CI 0·5–2·0]). Increased household transmission was associated with the delta and beta variants (vs wild-type, OR 10·4 [4·1–26·7] and 3·3 [1·4–8·2], respectively) and increased SARS-CoV-2 viral load in the index case (OR 5·3 [2·3–12·4]). Additionally, people living with HIV who had unsuppressed HIV viral loads (≥400 viral load copies per mL) were more likely to have symptomatic infection (OR 3·3 [1·3–8·4]), with longer shedding of SARS-CoV-2 (hazard ratio 0·4 [95% CI 0·3–0·6]), than HIV-uninfected individuals. This chronic persistent SARS-CoV-2 infection in patients with immunosuppression from uncontrolled HIV infection might promote the emergence of new variants.

Therefore, strengthening of antiretroviral treatment programmes is urgently needed, so that patients with advanced immunosuppression are prioritised for effective antiretroviral treatment and COVID-19 vaccination.

We think this study provides unique insights into the epidemiology of household transmission of SARS-CoV-2, in a largely unvaccinated population. The high prevalence of asymptomatic infection with similar transmission potential as symptomatic cases, and the need for frequent testing to detect transient infections, highlights the limitations and complexities of current screening and testing protocols. Symptom and temperature screening at entry points (eg, restaurants, schools, airports) might not have the public health infection containment benefit that was expected. Similarly, attempting to prevent nosocomial COVID-19 transmission by symptom and PCR screening on admission to hospital might miss transient infections if tests are not repeated regularly, given that patients with COVID-19 might not have symptoms, and transmission might have already occurred, despite a negative PCR test.

Current public health approaches encourage a combination of vaccination and non-pharmacological measures such as wearing a face mask, social distancing, hand sanitation, and ventilation strategies to prevent COVID-19 transmission.

This study suggests that the COVID waves in South Africa were potentially driven by household transmission in the young population, highlighting the difficulty in relying on non-pharmacological interventions as prevention and containment measures. At this time, vaccination remains the key public health intervention in high-risk populations that can provide immunity, and thus mitigate and limit severe infections, complications, and mortality from COVID-19.  
<https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00137-2/fulltext>

**title:** COVID-19 Vaccination and Access to the Organ Transplant Waiting List

JAMA | 18th march 2022   
  
As the co-leads for the American Society of Transplant Surgeons’ COVID-19 Strike Force for more than 2 years, we had hoped that this perspective would never be necessary. Yet, the SARS-CoV-2 virus continues to be a health care problem throughout the US, affecting the candidates, recipients, and donors of organ transplants, the transplant staff, and, to a variable degree, every hospital and every person in the country. Although therapeutic options have increased, the best available tool to mitigate the severity of COVID-19 disease is vaccination. It has been the COVID Strike Force’s consistent recommendation that all candidates, recipients (and family members), and live donors of organ transplant, in addition to transplant staff and physicians, receive an approved vaccine. This recommendation is to permit the continued practice of clinical organ transplant procedures with the lowest morbidity risk to the candidates, recipients, and those of us who care for them. Some centers (ours included) have made a policy that requires SARS-CoV-2 vaccination before a candidate’s registration on the national organ waiting list. The arguments for vaccine mandates are numerous1 but have been polarizing. Where does a requirement for SARS-CoV-2 vaccination fit within the current practice of organ transplant? Context for this recommendation requires an expanded scope for better understanding…  
<https://jamanetwork.com/journals/jamasurgery/fullarticle/2790274>

**title:** Durability of the Single-Dose Ad26.COV2.S Vaccine in the Prevention of COVID-19 Infections and Hospitalizations in the US Before and During the Delta Variant Surge

jama | 17th march 2022  
  
Question What is the durability of the Ad26.COV2.S COVID vaccine effectiveness before and during the Delta variant surge in the US?

Findings Among 422 034 vaccinated and 1 645 397 matched unvaccinated individuals across the US, vaccine effectiveness was estimated to be 76% for COVID-19 infection and 81% for hospitalizations for at least 180 days after vaccination before and during the Delta variant surge.

Meaning In this study, the Ad26.COV2.S COVID-19 vaccine was associated with high and durable effectiveness in clinical practice, including against the Delta variant.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790204>

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

jama oncology | 10th march 2022  
  
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.  
  
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.  
<https://www.nejm.org/doi/full/10.1056/NEJMoa2116414>

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

the lancet | 9th march 2022  
  
Background: 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.

Methods: In this single-blind, multicenter, randomized, controlled trial involving health care workers who had received a priming dose of Ad26.COV2.S vaccine, we assessed immunogenicity and reactogenicity 28 days after a homologous or heterologous booster vaccination. The participants were assigned to receive no booster, an Ad26.COV2.S booster, an mRNA-1273 booster, or a BNT162b2 booster. The primary end point was the level of S-specific binding antibodies, and the secondary end points were the levels of neutralizing antibodies, S-specific T-cell responses, and reactogenicity. A post hoc analysis was performed to compare mRNA-1273 boosting with BNT162b2 boosting.

Results: Homologous or heterologous booster vaccination resulted in higher levels of S-specific binding antibodies, neutralizing antibodies, and T-cell responses than a single Ad26.COV2.S vaccination. The increase in binding antibodies was significantly larger with heterologous regimens that included mRNA-based vaccines than with the homologous booster. The mRNA-1273 booster was most immunogenic and was associated with higher reactogenicity than the BNT162b2 and Ad26.COV2.S boosters. Local and systemic reactions were generally mild to moderate in the first 2 days after booster administration.

Conclusions: 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:** Comparing Human Milk Antibody Response After 4 Different Vaccines for COVID-19

jama pedatrics | 14th march 2022  
  
…We demonstrated that SARS-CoV-2–specific IgA in human milk was present more frequently after vaccination with an mRNA-based vaccine compared with a vector-based vaccine. Additionally, IgG was present in all participants after receiving 2 vaccine doses, independent of vaccine type. However, IgG was detectable earlier after vaccination with either of the mRNA vaccines, which can be explained by timing of the second dose. A limitation of this study is that we did not measure neutralizing capacity of the human milk antibodies.

The most abundant antibody in human milk is IgA, which plays a key role in the first line of defense against invading viruses.5 Although, to our knowledge, no studies have shown indisputable evidence that human-milk IgA directly protects against respiratory tract infections, it is very likely that this antibody plays a critical role. Based on these data, we suggest that an mRNA-based vaccine is the optimal choice for lactating women when they want to transfer antibodies to their infants. <https://jamanetwork.com/journals/jamapediatrics/fullarticle/2789947>

**title:** COVID-19 vaccine dose sparing: strategies to improve vaccine equity and pandemic preparedness

the lancet global health | 1st april 2022  
  
…Despite tremendous efforts, worldwide COVID-19 vaccination coverage is lagging. Dose-sparing strategies for COVID-19 vaccines can increase vaccine availability to address the global crisis. Several clinical trials evaluating dose sparing are currently underway. However, to rapidly provide solid scientific justification for different dose-sparing strategies, joint coordinated action involving both public and private parties is needed. In this Viewpoint, we provide examples of approaches to vaccine dose-sparing that have previously been evaluated in clinical trials to improve vaccine availability and reflect on the origin of their funding. With a focus on the current COVID-19 pandemic, we stress the need for expedited testing of vaccine dose-sparing strategies in endemic or epidemic infectious diseases. However, we argue that the establishment of a mechanism through which dose-sparing opportunities are systematically identified, scientifically tested, and ultimately implemented will prove to be valuable beyond the current pandemic for infectious diseases product development and pandemic preparedness in the future.  
<https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00075-4/fulltext>

**title:** Humoral responses after second and third SARS-CoV-2 vaccination in patients with immune-mediated inflammatory disorders on immunosuppressants: a cohort study

the lancet rheumatology | 17th march 2022  
  
Humoral responses following vaccination are impaired by specific immunosuppressants. After standard vaccination regimens, patients with immune-mediated inflammatory disorders taking most immunosuppressants show similar seroconversion to controls, although antibody titres might be moderately reduced. As neutralisation capacity and recall responses are also preserved in these patients, this is not likely to translate to loss of (short-term) protection. In patients on immunosuppressants showing poor humoral responses after standard vaccination regimens, a third vaccination resulted in additional seroconversion in patients taking mycophenolate mofetil combination treatments, whereas the effect of a third vaccination in patients on anti-CD20 therapy and S1P modulators was limited.  
<https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00034-0/fulltext>

**title:** Humoral response following SARS-CoV-2 vaccination: not all immunosuppressants are created equal

the lancet rheumatology | 17th march 2022  
  
…A study in The Lancet Rheumatology by Luuk Wieske and colleagues adds to existing evidence that humoral responses after standard vaccination (defined as two-dose ChAdOx1 nCoV-19 [Oxford–AstraZeneca], BNT162b2 [Pfizer–BioNtech], CX-024414 [Moderna], or single-dose Ad.26.COV2.S [Janssen]) are suboptimal among patients with immune-mediated inflammatory diseases treated with anti-CD20 therapy, sphingosine 1-phosphate receptor (S1P) modulator, or mycophenolate mofetil combination therapies. Similar rates of seroconversion were observed among patients treated with other immunosuppressants, although antibody titres were moderately reduced compared with controls. Given findings of a preserved recall response in these patients, the authors conclude that reduced antibody titres are unlikely to translate to loss of short-term protection. However, we believe that this conclusion might be premature in the absence of clinical outcome data, and more importantly, studies have demonstrated the correlation between antibody titres and breakthrough infections.

Moreover, recent data have highlighted that significantly higher antibody concentrations are required to overcome immune evasion induced by variants of concern, further underlining the potential role of antibody titres in guiding strategies for infection prevention…  
<https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00066-2/fulltext>

**workforce well-being**

**title:** Covid-19: NHS staff absences rise again as cases increase

BMJ | 18th march 2022  
  
NHS leaders have expressed concern after the latest figures showed that staff absences in hospitals were rising again amid high SARS-CoV-2 infection rates.

The figures, published by NHS England on 17 March,1 show that the number of staff in acute care trusts who were absent from work for covid related reasons increased by almost a fifth in the past week.

Seven day averages showed that covid related absences rose by 19% from 14 822 on 6 March to 17 579 on 13 March. The proportion of overall staff absences that were related to covid increased from 27% to 30% in the same week.

The number of staff absences that were due to covid remains much lower than the winter peak in early January, when in the week ending 9 January an average of 45 736 staff in hospitals were off. But Layla McCay, director of policy at the NHS Confederation, said the situation was nevertheless increasing pressure on hospitals and would have a knock-on effect on other services.  
<https://www.bmj.com/content/376/bmj.o737>

**recovery: HEALTH MANgement**

**title:** WHO Releases Report on Maintaining Health Services During COVID-19

jama | 15th march 2022   
  
A recent World Health Organization (WHO) report examines how 19 countries worked to mitigate COVID-19’s effects on providing maternal, newborn, child and adolescent, and aging health services.

The report is based on an initiative launched in May 2020 that brought experts in the countries together to form technical working groups with WHO support. The groups collected, synthesized, and analyzed information on mitigation strategies and how the countries used internal data for decision-making.

Through February 2021, the initiative found that countries varied widely in their specific service use from 2019 to 2020. For example, the number of births in health facilities—a category potentially affected by COVID-19 restrictions on travel and in-person encounters—remained stable or increased slightly in Cameroon, the Democratic Republic of the Congo, Ethiopia, South Africa, and Uganda. In Pakistan and Yemen, the number initially declined but recovered by the end of 2020 while the number declined without recovering in Nigeria and Sudan.

Similar patterns were recorded for antenatal care visits and visits for acute respiratory infections (ARIs) for children younger than 5 years. However, data interpretation was complicated by inconsistent reporting and a failure to determine whether ARIs were down because of COVID-19–related disruptions in care or reduced infection rates due to mask use and social distancing.

Overall, more interventions were aimed at maintaining maternal and child health services than aging services. Mobile service delivery, telehealth, enhanced infection control, and personal protective equipment use were frequent mitigation measures.  
<https://jamanetwork.com/journals/jama/fullarticle/2789956>

**title:** Trends in Hospitalizations for Ambulatory Care–Sensitive Conditions During the COVID-19 Pandemic

jama | 17th march 2022

Question How has the rate of potentially preventable hospitalizations (ambulatory care–sensitive conditions) changed during the COVID-19 pandemic?

Findings This cross-sectional study found statistically significant decreases in rates of potentially preventable hospitalizations during the pandemic relative to the prepandemic period but no significant change in the intensity of care provided during these admissions. These decreases are similar in magnitude to the overall decrease in non–COVID-19–related hospital admissions during the pandemic.

Meaning This study suggests that researchers should be cautious in interpreting changes in rates of potentially preventable hospitalizations during the pandemic as being solely due to the quality of ambulatory care because these rates are also likely due to other patient-level and hospital-level factors that are associated with the demand for hospital services.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790207>

**title:** A roadmap of recovery for the COVID generation

the lancet child & adolescent health | 1st april 2022

Many countries are declaring an end to this phase of the covid-19 pandemic, yet the underlying   
…The pandemic has had wide-ranging and long-lasting effects on young people, but children's developmental plasticity and resilience give us room for optimism. As the world moves into the next phase of pandemic recovery and living with COVID-19, we must grasp this opportunity to support every child to catch up and thrive. The Lancet Child & Adolescent Health will be publishing a Commission to build a roadmap of recovery for this COVID generation. We call for collaborators and research from all aspects of child and adolescent health—particularly from our colleagues in development, social science, and adolescent health—to join us.  
<https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(22)00070-0/fulltext>

**title:** Living In A Covid World: A Long-Term Approach To Resilience And Wellbeing

the house of lords covid-19 committee | 16th march 2022

This report concludes that the pandemic has shown that our current understanding of resilience and preparedness is not fit-for-purpose. It sets out a range of recommendations to improve resilience and preparedness, reconsider the role and purpose of the state, and move from a Welfare State to a Wellbeing State. The purpose of the Wellbeing State would be to secure the wellbeing of all its citizens, and tackle those inequalities that hold back specific groups and communities.  
<https://kingsfund.blogs.com/health_management/2022/03/living-in-a-covid-world-a-long-term-approach-to-resilience-and-wellbeing.html>

**title:** UK Covid-19 Inquiry: Draft Terms Of Reference

DHSC | 15th march 2022

The draft terms of reference set out the aims of the UK Covid-19 Inquiry. This follows consultation with the Inquiry Chair, Baroness Hallett, and ministers in the devolved administrations. A final terms of reference will be published once Baroness Hallett has consulted with the public, including with bereaved families and other affected groups. The public consultation on the inquiry’s terms of reference is now open and responses can be submitted on the UK Covid-19 Inquiry website. The consultation will close at 23:59pm on 7 April 2022.  
<https://kingsfund.blogs.com/health_management/2022/03/uk-covid-19-inquiry-draft-terms-of-reference.html>

**title:** Preventing exacerbations of chronic respiratory diseases

BMJ | 17th march 2022

Interventions intended to interrupt transmission of SARS-CoV-2 led to a striking fall in the incidence of common seasonal respiratory viral infections and an unexpected but equally striking fall in the incidence of acute exacerbations of pre-existing respiratory diseases. Many of these interventions aren’t sustainable, but it’s worth asking how habits should change in the post-pandemic era. We should at least be aware of the risk that apparently trivial colds pose to vulnerable individuals (Am J Respir Crit Care Med doi:10.1164/rccm.202110-2389CI).  
<https://www.bmj.com/content/376/bmj.o620>

**title:** Respiratory viruses evolve to become milder

BMJ | 17th march 2022

Virologists warn that it’s wishful thinking to believe that viruses evolve to become milder. Although the omicron variant of SARS-CoV-2 has been less severe than the delta variant, the next variant could easily be more deadly. However, it is advantageous for viruses transmitted by droplets and aerosols to keep their hosts well enough and mobile enough to come into contact with other susceptible hosts. If mutations are as likely to make a disease more dangerous as milder, why have rhinoviruses never turned into killers? (https://www.spectator.co.uk/article/breathe-easy-how-respiratory-viruses-evolve-to-become-milder)  
<https://www.bmj.com/content/376/bmj.o620>

**title:** Grandparents

BMJ | 17th march 2022

“Don’t kill Granny” became a slogan to encourage social distancing in England in the early months of 2021. As an essay in Scientific American points out, killing grannies is exactly what the pandemic has done. Most covid related deaths have occurred in people who are grandparents. This will have longlasting implications for childcare and family welfare (https://www.scientificamerican.com/article/the-devastating-loss-of-grandparents-among-one-million-covid-dead/).  
<https://www.bmj.com/content/376/bmj.o620>

**HEALTH INEQUALITIES & public health**

**title:** Acute COVID-19 severity and mental health morbidity trajectories in patient populations of six nations: an observational study

the lancet public health |14th march 2022  
  
Long-term mental and physical health consequences of COVID-19 (long COVID) are a persistent public health concern. Little is still known about the long-term mental health of non-hospitalised patients with COVID-19 with varying illness severities. Our aim was to assess the prevalence of adverse mental health symptoms among individuals diagnosed with COVID-19 in the general population by acute infection severity up to 16 months after diagnosis.

Methods: This observational follow-up study included seven prospectively planned cohorts across six countries (Denmark, Estonia, Iceland, Norway, Sweden, and the UK). Participants were recruited from March 27, 2020, to Aug 13, 2021. Individuals aged 18 years or older were eligible to participate. In a cross-sectional analysis, we contrasted symptom prevalence of depression, anxiety, COVID-19-related distress, and poor sleep quality (screened with validated mental health instruments) among individuals with and without a diagnosis of COVID-19 at entry, 0–16 months from diagnosis. In a cohort analysis, we further used repeated measures to estimate the change in mental health symptoms before and after COVID-19 diagnosis.

Findings: The analytical cohort consisted of 247 249 individuals, 9979 (4·0%) of whom were diagnosed with COVID-19 during the study period. Mean follow-up was 5·65 months (SD 4·26). Participants diagnosed with COVID-19 presented overall with a higher prevalence of symptoms of depression (prevalence ratio [PR] 1·18 [95% CI 1·03–1·36]) and poorer sleep quality (1·13 [1·03–1·24]) but not symptoms of anxiety (0·97 [0·91–1·03]) or COVID-19-related distress (1·05 [0·93–1·20]) compared with individuals without a COVID-19 diagnosis. Although the prevalence of depression and COVID-19-related distress attenuated with time, individuals diagnosed with COVID-19 but never bedridden due to their illness were consistently at lower risk of depression (PR 0·83 [95% CI 0·75–0·91]) and anxiety (0·77 [0·63–0·94]) than those not diagnosed with COVID-19, whereas patients who were bedridden for more than 7 days were persistently at higher risk of symptoms of depression (PR 1·61 [95% CI 1·27–2·05]) and anxiety (1·43 [1·26–1·63]) than those not diagnosed throughout the study period.

Interpretation: Severe acute COVID-19 illness—indicated by extended time bedridden—is associated with long-term mental morbidity among recovering individuals in the general population. These findings call for increased vigilance of adverse mental health development among patients with a severe acute disease phase of COVID-19.  
<https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(22)00042-1/fulltext>

**title:** Covid-19: Campaigners accuse Pfizer of blocking access to antiviral for trials in poorer countries  
  
BMJ | 17th MARCH 2022  
  
Pfizer has been accused of blocking “urgently needed” studies into the use of its novel oral antiviral drug for covid-19 combined with other medicines for use in low and middle income countries.

The Drugs for Neglected Diseases initiative (DNDi) expressed concern on behalf of a consortium of 26 African and global research bodies that the drug company would not provide access to Paxlovid.1 It said that the refusal to cooperate set a “dangerous precedent” given the number of other antivirals in the pipeline and that it was difficult to understand the rationale for the decision in a global pandemic.

At least three separate requests are understood to have been made to Pfizer, but despite several discussions a breakthrough has not been forthcoming. Around 1000 doses of the therapy would be required for the studies.  
<https://www.bmj.com/content/376/bmj.o721>

**title:** Covid-19: Doctors urge government to step up on global vaccine funding

BMJ | 17th march 2022  
  
A group of influential NHS doctors and medical bodies have called on the government to provide more funding to boost global covid-19 vaccination efforts. In a letter to Prime Minister Boris Johnson, they argue that the UK must play a bigger role and donate £720m to ensure that the World Health Organization’s target of vaccinating 70% of the world against covid-19 by summer is met. The #vaccinatetheworld campaign, which was started by a group of GPs and other NHS clinicians and leaders, is backed by more than 130 healthcare organisations including 10 royal colleges and the Faculty of Public Health. They note that the domestic covid-19 response has cost £360bn and that the amount they are asking the UK to contribute to the international community equates to just 0.036% of gross domestic product.  
<https://www.bmj.com/content/376/bmj.o709>

**title:** Alcohol-Related Deaths During the COVID-19 Pandemic

who europe | 11th march 2022  
  
This report showcases the work of WHO/Europe’s Covid-19 Incident Management Support Team   
Research suggests that alcohol consumption and related harms increased during the first year of the COVID-19 pandemic. Studies reported increases in drinking to cope with stress,1 transplants for alcohol-associated liver disease,2 and emergency department visits for alcohol withdrawal.3 We examined mortality data to assess whether alcohol-related deaths increased during the pandemic as well.

Methods: US mortality data from the National Center for Health Statistics were used to compare numbers and rates of alcohol-related and all-cause deaths among all individuals 16 years or older in 2019 and 2020. Provisional data for the first half of 2021 (as of January 2022) were obtained from the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research…

…The number and rate of alcohol-related deaths increased approximately 25% between 2019 and 2020, the first year of the COVID-19 pandemic. Rates increased prior to the pandemic, but less rapidly (2.2% mean annual percent change between 1999 and 20174). The rate increase for alcohol-related deaths in 2020 outpaced the increase in all-cause mortality, which was 16.6%. Previous reports suggest the number of opioid overdose deaths increased 38% in 2020, with a 55% increase in deaths involving synthetic opioids such as fentanyl.5 There were similar increases in the number of deaths in which alcohol contributed to overdoses of opioids (40.8%) and, specifically, synthetic opioids (59.2%). Deaths involving alcohol reflect hidden tolls of the pandemic. Increased drinking to cope with pandemic-related stressors, shifting alcohol policies, and disrupted treatment access are all possible contributing factors.1 Whether alcohol-related deaths will decline as the pandemic wanes, and whether policy changes could help reduce such deaths, warrants consideration.

Study limitations include inaccurate death certificates, such as underreporting of alcohol involvement,6 and unclear causal relationships among listed causes of deaths. Provisional data are subject to change when more death certificates are processed.  
<https://jamanetwork.com/journals/jama/fullarticle/2790491>

**title:** Assessment of a Crisis Standards of Care Scoring System for Resource Prioritization and Estimated Excess Mortality by Race, Ethnicity, and Socially Vulnerable Area During a Regional Surge in COVID-19

jama | 15th march 2022  
  
Question Is a crisis standards of care scoring system designed to allocate scarce resources in the COVID-19 pandemic associated with inequities in resource allocation by race?

Findings In this cohort study of 498 adults admitted to the intensive care unit and preemptively scored during a COVID-19 surge, nearly twice the proportion of Black patients were scored in the lowest priority group compared with all other patients, a significant difference.

Meaning These findings suggest that a scoring system designed to maximize lives and life-years saved in the setting of resource scarcity during the COVID-19 pandemic may result in racial inequities in prioritization.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790104>

**title:** Polarized Public Opinion About Public Health During the COVID-19 Pandemic: Political Divides and Future Implications

jama | 18th march 2022  
  
In recent years, political polarization in the US has grown, and this polarization is being reflected in the public’s attitudes toward the field of public health, which was traditionally considered to be science-based and nonpartisan. Understanding the extent of polarization in public opinion is crucial to guide public health and policy leaders. We reviewed the results of 6 nationally representative polls of US adults (≥18 years old) conducted during the COVID-19 pandemic (2020 and 2021) on the US public health system1-6 as well as a comparable poll conducted in 2009.7 We examined the gaps between Democrats’ and Republicans’ views and found stark differences in several areas with major implications for the future of public health.  
<https://jamanetwork.com/journals/jama-health-forum/fullarticle/2790248>

**title:** Inequitable Resource Allocation Amidst a Pandemic—A Crisis Within a Crisis

jama | 15th march 2022  
  
The COVID-19 pandemic has made us reconsider our approach to many aspects of health care. Two issues frequently discussed are the impact of systemic racism on access and outcomes as well as the need to establish practical and valid crisis standards of care (CSOC) policies to assist in resource allocation when demand exceeds supply. At their intersection is the possibility for inequitable triage, a humanmade crisis we cannot accept.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790110>

**international perspectives**

**title:** Covid-19: Hong Kong reports world’s highest death rate as zero covid strategy fails

BMJ| 17th march 2022  
  
Coronavirus infections are surging in Hong Kong as the city has reported the highest number of covid-19 deaths for population size in the world. Previously a global model for covid containment, transmission of SARS-CoV-2 has soared as Hong Kong’s zero covid strategy has failed to contain the more contagious omicron variant. The city’s low vaccine coverage is also aiding transmission and leading to more fatalities, said epidemiologists. Hong Kong’s isolation centres, hospitals, and morgues are overflowing, and some shops have empty shelves as residents are hoarding supplies in anticipation of a potential city-wide lockdown, the news agency Reuters has reported. The covid death rate in Hong Kong is now above 25 per 100 000 residents—higher than in the UK last December when the omicron variant first appeared…  
<https://www.bmj.com/content/376/bmj.o707>

**title:** Covid-19: Countries in the Americas are warned not to lower their guard

BMJ | 14th march 2022  
  
Covid-19 is on the retreat across the American continents but it is too early for the region to let its guard down, warned the Pan American Health Organisation, the World Health Organization’s regional office for the Americas, on 9 March. Reported cases of covid-19 fell by 26% in the past week and deaths by nearly 19%, as the omicron wave of infections tailed off. But ongoing transmission and future variants could expose the region’s public health priorities once more, said PAHO’s director, Carissa Etienne. A total of 2.6 million people have died from covid-19 in the Americas, the highest number of any region of the world and almost half of the global total, despite being home to only 13% of its population. “This is a tragedy of enormous proportions, and its effects will be felt for years to come,” said Etienne on the second anniversary of the pandemic…  
<https://www.bmj.com/content/376/bmj.o664>

**title:** Changes and Inequities in Adult Mental Health–Related Emergency Department Visits During the COVID-19 Pandemic in the US

jama psychiatry | 16th march 2022  
  
Question How have adult mental health (MH)–related emergency department (ED) visits changed during the COVID-19 pandemic?

Findings In this cross-sectional study of 107 761 319 eligible ED visits, MH-related visit count findings depended on the COVID-19 pandemic period examined, whether this was compared with other periods in the pandemic or prepandemic period, and which mental disorder was examined. There was between- and within-group variation in ED visits by race and ethnicity, which varied by pandemic period examined, and there were increases in some disorders after COVID-19 case peaks for adults aged 18 to 24 years.

Meaning Results of this study suggest that EDs may have increases in MH-related visits after COVID-19 surges, especially for young adults and some racial and ethnic minoritized subpopulations.  
<https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2790337>