COVID-19 weekly update

3rd May 2022

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**clinical management**

**title:** Diagnosis and management of covid-19 in pregnancy

BMJ| 26th april 2022

Abstract: Pregnant women with covid-19 are at greater risk of severe disease than their non-pregnant peers, and yet they are frequently denied investigations or treatments because of unfounded concerns about risk to the fetus. The basic principles of diagnosing and managing covid-19 are the same as for non-pregnant patients, and a multidisciplinary, expert team approach is essential to ensure optimal care. During pregnancy, treatment with corticosteroids should be modified to use non-fluorinated glucocorticoids. Il-6 inhibitors and monoclonal antibodies, together with specific antiviral therapies, may also be considered. Prophylaxis against venous thromboembolism is important. Women may require respiratory support with oxygen, non-invasive ventilation, ventilation in a prone position (either awake or during invasive ventilation), intubation and ventilation, and extracorporeal membrane oxygenation (ECMO). Pregnancy is not a contraindication for any of these supportive therapies, and the criteria for providing them are the same as in the general population. Decisions regarding timing, place, and mode of delivery should be taken with a multidisciplinary team including obstetricians, physicians, anesthetists, and intensivists experienced in the care of covid-19 in pregnancy. Ideally these decisions should take place in consultation with centers that have experience and expertise in all these specialties.
<https://www.bmj.com/content/377/bmj-2021-069739>

**title:** Association of SARS-CoV-2 Infection During Pregnancy With Maternal and Perinatal Outcomes

jama | 2nd may 2022

Question Is SARS-CoV-2 infection during pregnancy associated with increased risk of adverse maternal and perinatal outcomes?

Findings This Canadian surveillance study included 6012 completed pregnancies between March 2020 and October 2021. Among cases of infection during pregnancy compared with cases of infection among the general Canadian population of reproductive-age female individuals, there was a significantly increased risk of SARS-CoV-2–related hospitalization (relative risk, 2.65) and intensive care unit admission (relative risk, 5.46). Among cases of infection during pregnancy compared with pregnant individuals without SARS-CoV-2 infection, there was a significantly increased risk of preterm birth (relative risk, 1.63).

Meaning SARS-CoV-2 infection during pregnancy was significantly associated with increased risk of adverse maternal outcomes and preterm birth.
<https://jamanetwork.com/journals/jama/fullarticle/2792031>

title: COVID-19: WHAT IS THE EVIDENCE FOR THE ANTIVIRAL PAXLOVID?

BMJ| 27th april 2022

With clinical evidence behind it growing, the combination treatment is moving from the laboratory to patients around the world at record speed, reports Andy Extance

What is it? Paxlovid is an antiviral combination developed by the pharmaceutical giant Pfizer. The treatment includes the newly developed antiviral drug nirmatrelvir and ritonavir, a potent inhibitor of the cytochrome P450-3A4 (CYP3A4) enzyme that metabolises several classes of drugs. Ritonavir slows down nirmatrelvir’s breakdown, thereby increasing drug concentrations and delaying clearance. Patients take Paxlovid as three tablets, two 150 mg tablets of nirmatrelvir and one 100 mg tablet of ritonavir together, twice daily for five days. As with the covid antiviral treatment molnupiravir, the oral route of delivery makes it convenient to take at home, unlike some other drugs for covid-19, which require intravenous infusion.

Who is eligible for treatment? It is authorised for people older than 12 years old, weighing more than 40 kg, who have mild to moderate covid-19, and who are at high risk of progression to severe symptoms, hospital admission, or death. Treatment should start as soon as possible after diagnosis and within five days of the onset of symptoms. On 9 March this year Pfizer started a phase 2/3 trial in 140 children aged 18 or younger…
<https://www.bmj.com/content/377/bmj.o1037>

**title:** Covid-19: Stockpiling antivirals risks repeating Tamiflu mistakes, experts warn

BMJ| 27th april 2022

The UK government has made a huge investment in antivirals to fight covid, but some experts are concerned the waste and overspending of the 2000s will recur. Gareth Iacobucci reports

The government’s Antivirals Taskforce has procured more antivirals per population than any other country in Europe, with over 4.98 million courses ordered so far.1 Included within this is 2.75 million courses of Pfizer’s oral antiviral drug Paxlovid (a combination of nirmatrelvir and ritonavir tablets).

Andrew Hill, senior visiting research fellow in the Department of Pharmacology and Therapeutics at the University of Liverpool, has estimated, using publicly available drug prices in the US, that the UK has spent £2.2bn (€2.6bn; $2.8bn) so far on procuring antivirals. “There’s a vast amount of money involved,” he told The BMJ. “As usual, all government contracts are confidential, so maybe they got some discount. But if the UK paid US prices, which it has with vaccines, then it has spent around £2.2bn on antivirals for covid.”

Uncertain evidence. Yet, despite this huge investment, evidence for the effectiveness of antivirals remains uncertain. Last November Pfizer reported results from an interim analysis of phase 2/3 data showing that Paxlovid, the second oral antiviral drug for covid-19 to be authorised for use in the UK, can reduce the relative risk of death or hospital admission by 89%.2 The government has seized on these results to justify its investment. However, the data were based on unvaccinated participants, while most at-risk people in the UK who would be eligible to receive the drug have been vaccinated.

Early data indicate that Paxlovid could be more effective than molnupiravir, the first oral antiviral to be made available in the UK, with fewer safety concerns. The latest rapid recommendation from a WHO Guideline Development Group of international experts, published in The BMJ last week,5 strongly recommended Paxlovid for patients with non-severe covid-19 who are at the highest risk of hospital admission, such as unvaccinated, older, or immunosuppressed patients. But it made no recommendation for patients with severe or critical covid-19, as there are currently no trial data on Paxlovid for this group. Both studies that informed the recommendation (EPIC-SR and EPIC-HR) excluded patients with severe or critical illness, and all patients were unvaccinated.

The Panoramic trial

The UK’s large national Panoramic study, run by the University of Oxford in collaboration with hubs of general practices, is aiming to fill the gaps in the evidence base by assessing how antivirals work where most of the adult population is vaccinated.

For several months, Paxlovid has been available directly through the NHS to a limited number of people at higher risk of serious illness who test positive for SARS-CoV-2, including those who are immunocompromised, patients with cancer, and people with Down’s syndrome. This month Paxlovid was added to the Panoramic study and will now be offered to an additional 17 500 vulnerable people in England, in addition to the 23 000 previously recruited to the trial to receive molnupiravir.

Nick Lemoine, medical director at the National Institute for Health and Care Research, which is funding the study, said, “While smaller scale studies have already shown this new antiviral treatment to be highly effective against covid in the early stages of infection, additional evidence from much larger cohorts is needed to enable clinicians and health services to make best use of these exciting new treatments.”

Jumping the gun? Some experts are concerned that the government has jumped the gun by going ahead with stockpiling antivirals in such quantities when the evidence is still uncertain. Hill said, “If the drug fails in Panoramic, can the UK get the money back? And how do you justify spending a 10th of the entire NHS drug budget on drugs that might not work at all? It could be used much more wisely elsewhere. “I think there are a lot of parallels with Tamiflu, and it could be a repeat. With Tamiflu [and Relenza] the government wasted £600m. This time we’re talking £2.2bn.”

In a recent editorial published in The BMJ, James Brophy, professor of medicine and epidemiology at McGill University, Montreal, argued that molnupiravir was authorised too early for covid patients and without sufficient evidence of its effectiveness.7 He told The BMJ that although the situation was less clear cut with Paxlovid he held similar concerns. “There is so much uncertainty as to what is the actual effect size [in the EPIC-SR trial], especially in vaccinated people,” he said.

Brophy attributes the early stockpiling to what he bluntly calls a “‘cover our ass’ mentality, which says, ‘Let’s look like we are doing something even if we aren’t sure it works and it costs a fortune, since we don’t want to be criticised.’”

“No apologies” When asked by The BMJ whether it would be able to recoup any of the money spent on procuring Paxlovid if the drug was shown not to be effective in the Panoramic trial, the Department of Health and Social Care for England said that details on costs and the recuperation of drugs were commercially sensitive. A department spokesperson said, “We have secured more lifesaving antivirals per head than any other country in Europe for NHS patients, and we make no apologies for doing so, given that our first priority is protecting patients. “Both antivirals have been shown to be highly effective in clinical trials, as well as by our renowned medicines regulator. For example, Paxlovid reduced the relative risk of hospitalisation or death due to covid by 88%. “The Panoramic study is collecting further data on how antivirals work in a vaccinated population, to inform the wider rollout later this year.”

Low uptake. Aside from the evidence for their effectiveness, it is also becoming apparent that supply of antivirals is exceeding demand, casting further doubt on the wisdom of stockpiling the drugs in such large quantities. Uptake in the UK is modest. NHS England said that around 32 000 patients had received antivirals since December, when they were introduced for people outside hospitals, and that only around 6000 had received Paxlovid as of 9 April.8 An analysis by Reuters showed that supply of Paxlovid has far outstripped demand in the UK, the US, Japan, and South Korea.9 Complex eligibility requirements, reduced availability of testing, and potential for drug interactions have all been cited as potential barriers.

Hill noted that the need to administer Paxlovid swiftly after infection was a major practical hurdle. “You have to start treating within five days the symptoms first appearing,” he said. “You get a lot of people who don’t know if it’s actually covid on the first day. Then you’ve got to get a test, then you’ve got to get a GP appointment at short notice, and then you’ve got to get a prescription. I’d suggest this is very hard for most people.” He added, “The other very serious issue with this drug is that it could actually cause more harm than good. It contains a booster drug called ritonavir, which causes drug interactions by increasing the concentrations of other drugs. In order for that not to happen, somebody has to have a very detailed review of all the patient’s comedications, which could take ages. That’s yet another barrier to somebody starting this drug.”
<https://www.bmj.com/content/377/bmj.o1053>

**title:** Molnupiravir might be dangerous without clarification of its indications [correspondence]

BMJ | 26th april 2022

The data on which the approval of molnupiravir was based in Japan and the data reported by Bernal et al are worrying and emphasise the huge unknowns around the use of molnupiravir.

The first problem is efficacy estimates that change substantially over time. In the interim analysis, the relative risk (RR) for hospital admission for any cause or death through day 29 was 0.52 (95% confidence interval 0.34 to 0.80). But the effect was less strong in the final analysis (RR 0.70 (0.49 to 0.99)).

A bigger problem is that the RR after interim analysis was 1.33 (0.69 to 2.54). The 95% confidence intervals for the before and after interim analysis overlap only slightly, and a significant difference between them cannot be ruled out. Moreover, the direction of the effect is different before and after the interim analysis. In the interim analysis, molnupiravir reduced the primary outcome, but afterwards it tended to increase it…
<https://www.bmj.com/content/377/bmj.o1030>

**title:** Imbalance in baseline characteristics in molnupiravir trials [correspondence]

bmj| 26th april 2022

Flawed research means we still do not know if the drug is safe or effective.
Brophy emphasises the dangers of making decisions based on a single prematurely terminated trial. The molnupiravir trials have several more problems:

-The risk of hospital admission or death associated with molnupiravir was not significant in the all randomised population when adjusted for sex (hazard ratio 0.69, 95% confidence interval 0.48 to 1.01).

-Molnupiravir may worsen covid-19 outcomes after the interim analysis—simply calculating the rate of hospital admission or death in the population of participants who were included in the final analysis but not the interim analysis shows that the molnupiravir group had a non-significant higher risk (6.2%) than the placebo group (4.7%).

-The Move-Out trial has serious imbalances in baseline risk factors that favour molnupiravir. Patients with chronic obstructive pulmonary disease were assigned at a significantly lower rate to the molnupiravir group (odds ratio 0.31, P=0.0043).4 The sum of the percentages of the participants with risk factors other than obesity was significantly lower in the molnupiravir group (43.4%) than in the placebo group (51.8%) (OR 0.71, P=0.019). With restriction to four risk factors (diabetes, chronic kidney disease, chronic obstructive pulmonary disease, and active cancer), risk was almost 40% lower in the molnupiravir group (OR 0.61, P=0.0043).4 These findings suggest that blinding might have been broken before the interim analysis.

-Significant imbalances (except obesity) were also observed in the all randomised population (OR=0.79, P=0.0314), which raises doubts about fair randomisation…
<https://www.bmj.com/content/377/bmj.o977>

**title:** Molnupiravir’s authorisation should be re-evaluated after the Panoramic trial is reported

BMJ | 26th april 2022

Brophy’s editorial on Merck’s Move-Out trial of molnupiravir raises important concerns about the approval of molnupiravir to treat outpatients with covid-19 in the United Kingdom.1 Molnupiravir has not yet been approved in Europe,2 and orders were recently cancelled in France.3

Molnupiravir reduced the risk of hospital admission or death by 52% versus placebo in the interim analysis but raised risk by 35% among patients subsequently evaluated.4 There was no clear explanation for this substantial disparity in treatment effects between the interim and final phases. Molnupiravir showed no overall benefit over placebo for resolution of covid-19 related signs and symptoms.5

Molnupiravir is now being evaluated in the UK Panoramic trial, coordinated by Oxford University (https://www.panoramictrial.org/). The inclusion criteria and primary efficacy endpoint are similar to the Move-Out trial, with two exceptions. Panoramic includes mainly vaccinated patients, and is being conducted during the Omicron wave, whereas Move-Out included only unvaccinated patients and was conducted in 2021, when previous variants led to more severe disease…
<https://www.bmj.com/content/377/bmj.o973>

**title:** Oral Antiviral Medications for COVID-19 [jama patient page]

jama| 25th april 2022

Two new oral antiviral medications are available for treatment of COVID-19. Two new antiviral medications, ritonavir-boosted nirmatrelvir (Paxlovid, ie, nirmatrelvir-ritonavir) and molnupiravir (Lagevrio), are currently available in the US under emergency use authorization. These 2 drugs are authorized for treatment of patients with mild to moderate COVID-19 who are not currently hospitalized but are at high risk of developing severe disease. Nirmatrelvir-ritonavir and molnupiravir are approved for use only within 5 days of onset of COVID-19 symptoms…
<https://jamanetwork.com/journals/jama/fullarticle/2791780>

**title:** Hepatitis in children: What’s behind the outbreaks?

BMJ| 26th april 2022

Cases of idiopathic hepatitis in children have been reported around the world. Elisabeth Mahase looks at what we know so far

How many children have been affected? The World Health Organization has so far reported 169 cases of acute hepatitis of unknown origin from 11 countries in Europe and the US, as of 21 April 2022. In the UK, where the increase in cases was first noted at the start of 2022, 114 cases have been confirmed, followed by 13 in Spain, 12 in Israel, nine in the US, six in Denmark, five in Ireland, four in the Netherlands and in Italy, two in Norway and in France, and one in Romania and in Belgium. Ages of the affected children range from 1 month to 16 years. Japan’s health ministry (25 April) has reported its first possible case in a child under the age of 17 who has been admitted to hospital.

Is this higher than normal? It seems to be. Will Irving, professor of virology at the University of Nottingham, told The BMJ that there had always been a background but low incidence of severe hepatitis in young children without a known cause but that now the numbers had risen fivefold to 10-fold. These cases are referred to as non-A-E hepatitis, because although the patients are known to have hepatitis, all the markers for the usual suspects—hepatitis A, B, C, and E—are negative. Irving said, “Normally a paediatric haematologist in, say, Birmingham, at one of the big UK centres, might see one or two cases a month. For many years we’ve wondered whether there was another virus that’s causing non-A-E hepatitis. There’s always a background level there, but now Birmingham, for example, has seen 40 cases in three months.”

How serious is it? Most children seem to be recovering well. However, WHO has confirmed that at least one child has died so far, while 17 children (around 10% of the total known cases) have needed a liver transplantation. Simon Taylor-Robinson, consultant hepatologist at Imperial College London, said, “Treatment is usually supportive, with hydration and management of temperature, because the problem normally resolves. The liver has an amazing ability to regenerate itself after an insult. Generally, within a few days or weeks, things settle back down with this supportive treatment. If blood tests are significantly abnormal, treatment would be in a specialised hospital, as in rare cases the liver injury can require more specialised medical intervention.”

Why is it happening? While there is no certain cause, the current hypothesis relates to adenovirus type 41, because many of the children with hepatitis have tested positive for this virus. Adenovirus 41 is known to infect children and cause symptoms such as diarrhoea, vomiting, and fever, although it has not previously been linked to hepatitis. In its latest report the UK Health Security Agency said it believed that there was a “cofactor affecting young children which is rendering normal adenovirus infections more severe or causing them to trigger immunopathology.”3 The report listed several possible cofactors, including susceptibility arising from lack of prior exposure during the pandemic; a prior infection with SARS-CoV-2 or another infection; a coinfection with SARS-CoV-2 or another infection; or a toxin, drug, or environmental exposure.

The agency suggested some other possible causes, although it noted that these did not fit as well with the current evidence. These included a novel variant of adenovirus, with or without a contribution from a cofactor as listed above; a drug, toxin, or environmental exposure; a novel pathogen either acting alone or as a coinfection; or a new variant of SARS-CoV-2.

Commenting on the current theories, Zania Stamataki, associate professor in viral immunology at the University of Birmingham, said, “The rising incidence of children with sudden onset hepatitis is unusual and worrying. If an adenovirus is to blame, this could be a new variant of adenovirus that may cause liver injury in children with naïve or immature immune systems. But we need to know more to be sure.“Alternatively, if adenovirus is the culprit for hepatitis in children who are otherwise well, we ought to look for other infections and environmental causes that could exacerbate adenoviral inflammation.”

Might the pandemic have played a role? Irving said that the covid pandemic could have had an effect, notably through the reduction in social mixing and virus spreading. “It is conceivable that whatever it was that was causing the odd case before is now, like all of the other viruses, simply circulating more widely because of the effects of lockdown and then the release from lockdown. “That’s an alternative hypothesis: that there’s always been a non-native virus that we haven’t yet identified and that that’s simply circulating at greater levels than it used to, because of the effects of the pandemic,” he told The BMJ.
<https://www.bmj.com/content/377/bmj.o1067>

**long-term effects**

**title:** Covid-19: Only a quarter of patients admitted to hospital feel fully recovered after a year, study finds

BMJ| 25th april 2022

Only around one in four people who had covid-19 reported feeling fully recovered within a year of being discharged from hospital, a study has found. The research, presented at the 2022 European Congress of Clinical Microbiology and Infectious Diseases held in Lisbon, Portugal, included 2320 patients discharged from NHS hospitals in the UK from March 2020 to April 2021. They were assessed at five months and at one year after discharge, with 807 (32.7%) completing both visits.

The study found that the proportion of patients reporting full recovery was practically unchanged between the two visits: 26% at five months (501 of 1965) and 29% at one year (232 of 804). Recovery was assessed using patient reported outcome measures, physical performance, and organ function at five months and at one year after hospital discharge. Blood samples were also taken at five months to check for the presence of various inflammatory proteins.

Factors associated with being less likely to report full recovery at one year were being female (odds ratio 0.68 (95% confidence interval 0.46 to 0.99)), being obese (0.50 (0.34 to 0.74)), and having had invasive mechanical ventilation (0.42 (0.23 to 0.76)).

Symptom severity. The research paper, published in the Lancet Respiratory Medicine,1 is part of the Post-Hospitalisation Covid-19 study, a national consortium led by experts at the University of Leicester and University Hospitals of Leicester NHS Trust to investigate the long term effects of covid-19 on health outcomes in patients who were admitted to hospital.

In an earlier paper from the same group the authors identified four clusters of symptom severity at five months,2 which have subsequently been confirmed at the one year mark by this latest study. Just over 1600 patients had sufficient data to allocate them to a cluster, with 319 (20%) having very severe physical and mental health impairment, 493 (30%) having severe physical and mental health impairment, 179 (11%) having moderate physical health impairment with cognitive impairment, and 645 (39%) having mild mental and physical health impairment.

The researchers found that being obese, having reduced exercise capacity, a greater number of symptoms, and increased levels of the inflammatory biomarker C reactive protein were all associated with the more severe clusters. Levels of the inflammatory biomarker interleukin 6 (IL 6) were also found to be higher in the “very severe” and the “moderate with cognitive impairment” clusters than in the “mild” cluster.

Louise Wain, one of the study authors who is an epidemiologist and GSK/British Lung Foundation chair in respiratory research at the University of Leicester, said, “No specific therapeutics exist for long covid, and our data highlight that effective interventions are urgently required. Our findings of persistent systemic inflammation, particularly in those in the very severe and moderate with cognitive impairment clusters, suggest that these groups might respond to anti-inflammatory strategies . . .

“The finding also suggests the need for complex interventions that target both physical and mental health impairments to alleviate symptoms. However, specific therapeutic approaches to manage post-traumatic stress disorder might also be needed.”

A paper describing the longest known covid-19 infection—a patient who tested positive for 505 days before dying—was also presented at the conference. The previous longest confirmed case was believed to be 335 days.3
<https://www.bmj.com/content/377/bmj.o1043>

**title:** Parosmia—a common consequence of covid-19

BMJ| 27th april 2022

What you need to know

•-Parosmia is a common sequelae of smell loss associated with covid-19, with onset on average three months after initial infection

•-Refer patients with parosmia without a clear preceding cause such as covid-19 and those with red flag symptoms

•-The presence of parosmia is positively associated with better outcomes from olfactory training in patients with loss of sense of smell—they are more likely to regain their sense of smell than those without parosmia…
<https://www.bmj.com/content/377/bmj-2021-069860>

**title:** Development and validation of the symptom burden questionnaire for long covid (SBQ-LC): Rasch analysis

BMJ| 27th april 2022

Objective To describe the development and validation of a novel patient reported outcome measure for symptom burden from long covid, the symptom burden questionnaire for long covid (SBQ-LC).

Design Multiphase, prospective mixed methods study. Setting Remote data collection and social media channels in the United Kingdom, 14 April to 1 August 2021. Participants 13 adults (aged ≥18 years) with self-reported long covid and 10 clinicians evaluated content validity. 274 adults with long covid field tested the draft questionnaire.

Main outcome measures Published systematic reviews informed development of SBQ-LC’s conceptual framework and initial item pool. Thematic analysis of transcripts from cognitive debriefing interviews and online clinician surveys established content validity. Consensus discussions with the patient and public involvement group of the Therapies for Long COVID in non-hospitalised individuals: From symptoms, patient reported outcomes and immunology to targeted therapies (TLC Study) confirmed face validity. Rasch analysis of field test data guided item and scale refinement and provided initial evidence of the SBQ-LC’s measurement properties.

Results SBQ-LC (version 1.0) is a modular instrument measuring patient reported outcomes and is composed of 17 independent scales with promising psychometric properties. Respondents rate their symptom burden during the past seven days using a dichotomous response or 4 point rating scale. Each scale provides coverage of a different symptom domain and returns a summed raw score that can be transformed to a linear (0-100) score. Higher scores represent higher symptom burden. After rating scale refinement and item reduction, all scales satisfied the Rasch model requirements for unidimensionality (principal component analysis of residuals: first residual contrast values <2.00 eigenvalue units) and item fit (outfit mean square values within 0.5 -1.5 logits). Rating scale categories were ordered with acceptable category fit statistics (outfit mean square values <2.0 logits). 14 item pairs had evidence of local dependency (residual correlation values >0.4). Across the 17 scales, person reliability ranged from 0.34 to 0.87, person separation ranged from 0.71 to 2.56, item separation ranged from 1.34 to 13.86, and internal consistency reliability (Cronbach’s alpha) ranged from 0.56 to 0.91.

Conclusions SBQ-LC (version 1.0) is a comprehensive patient reported outcome instrument developed using modern psychometric methods. It measures symptoms of long covid important to people with lived experience of the condition and may be used to evaluate the impact of interventions and inform best practice in clinical management.
<https://www.bmj.com/content/377/bmj-2022-070230>

**title:** Long-term mortality following SARS-CoV-2 infection: A national cohort study from Estonia

the lancet regional health europe| 28th april 2022

Background. The objective of this study was to describe 12-month mortality following SARS-CoV-2 infection compared with a reference population with no history of SARS-CoV-2.

Methods. Nationwide cohort study using electronic health care data on SARS-CoV-2 RNA positive cases (n= 66,287) and reference group subjects (n=254,969) with linkage to SARS-CoV-2 testing and death records.

Findings. People infected with SARS-COV-2 had more than three times the risk of dying over the following year compared with those who remained uninfected (aHR 3·1, 95%CI 2·9-3·3). Short-term mortality (up to 5 weeks post-infection) was significantly higher among COVID-19 group (1623·0/10 000) than in the reference group (118/10 000). For COVID-19 cases aged 60 years or older, increased mortality persisted until the end of the first year after infection, and was related to increased risk for cardiovascular (aHR 2·1, 95%CI 1·8-2·3), cancer (aHR 1·5, 95%CI 1·2-1·9), respiratory system diseases (aHR 1·9, 95%CI 1·2-3·0), and other causes of death (aHR 1·8, 95%CI 1·4-2·2).

Interpretation. Increased risk of death from SARS-CoV-2 is not limited to the acute illness: SARS-CoV-2 infection carries a substantially increased mortality in the following 12 months. This excess death mainly occurs in older people and is driven by broad array of causes of death.
[https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00087-4/fulltext](https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762%2822%2900087-4/fulltext)

**title:** Multivariate profile and acute-phase correlates of cognitive deficits in a COVID-19 hospitalised cohorT

the lancet eclinical medicine| 28th april 2022

Background. Preliminary evidence has highlighted a possible association between severe COVID-19 and persistent cognitive deficits. Further research is required to confirm this association, determine whether cognitive deficits relate to clinical features from the acute phase or to mental health status at the point of assessment, and quantify rate of recovery.

Methods. 46 individuals who received critical care for COVID-19 at Addenbrooke's hospital between 10th March 2020 and 31st July 2020 (16 mechanically ventilated) underwent detailed computerised cognitive assessment alongside scales measuring anxiety, depression and post-traumatic stress disorder under supervised conditions at a mean follow up of 6.0 (± 2.1) months following acute illness. Patient and matched control (N = 460) performances were transformed into standard deviation from expected scores, accounting for age and demographic factors using N = 66,008 normative datasets. Global accuracy and response time composites were calculated (G\_SScore & G\_RT). Linear modelling predicted composite score deficits from acute severity, mental-health status at assessment, and time from hospital admission. The pattern of deficits across tasks was qualitatively compared with normal age-related decline, and early-stage dementia.

Findings. COVID-19 survivors were less accurate (G\_SScore=-0.53SDs) and slower (G\_RT=+0.89SDs) in their responses than expected compared to their matched controls. Acute illness, but not chronic mental health, significantly predicted cognitive deviation from expected scores (G\_SScore (p=​​0.0037) and G\_RT (p = 0.0366)). The most prominent task associations with COVID-19 were for higher cognition and processing speed, which was qualitatively distinct from the profiles of normal ageing and dementia and similar in magnitude to the effects of ageing between 50 and 70 years of age. A trend towards reduced deficits with time from illness (r∼=0.15) did not reach statistical significance.

Interpretation. Cognitive deficits after severe COVID-19 relate most strongly to acute illness severity, persist long into the chronic phase, and recover slowly if at all, with a characteristic profile highlighting higher cognitive functions and processing speed.
[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(22)00147-X/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370%2822%2900147-X/fulltext)

**title:** An online breathing and wellbeing programme (ENO Breathe) for people with persistent symptoms following COVID-19: a parallel-group, single-blind, randomised controlled trial

the lancet respiratory medicine| 27th april 2022

Background. There are few evidence-based interventions for long COVID; however, holistic approaches supporting recovery are advocated. We assessed whether an online breathing and wellbeing programme improves health related quality-of-life (HRQoL) in people with persisting breathlessness following COVID-19.

Methods. We conducted a parallel-group, single-blind, randomised controlled trial in patients who had been referred from one of 51 UK-based collaborating long COVID clinics. Eligible participants were aged 18 years or older; were recovering from COVID-19 with ongoing breathlessness, with or without anxiety, at least 4 weeks after symptom onset; had internet access with an appropriate device; and were deemed clinically suitable for participation by one of the collaborating COVID-19 clinics. Following clinical assessment, potential participants were given a unique online portal code. Participants were randomly assigned (1:1) to either immediate participation in the English National Opera (ENO) Breathe programme or to usual care. Randomisation was done by the research team using computer-generated block randomisation lists, with block size 10. The researcher responsible for randomisation was masked to responses. Participants in the ENO Breathe group participated in a 6-week online breathing and wellbeing programme, developed for people with long COVID experiencing breathlessness, focusing on breathing retraining using singing techniques. Those in the deferred group received usual care until they exited the trial. The primary outcome, assessed in the intention-to-treat population, was change in HRQoL, assessed using the RAND 36-item short form survey instrument mental health composite (MHC) and physical health composite (PHC) scores. Secondary outcome measures were the chronic obstructive pulmonary disease assessment test score, visual analogue scales (VAS) for breathlessness, and scores on the dyspnoea-12, the generalised anxiety disorder 7-item scale, and the short form-6D. A thematic analysis exploring participant experience was also conducted using qualitative data from focus groups, survey responses, and email correspondence. This trial is registered with ClinicalTrials.gov, NCT04830033.

Findings. Between April 22 and May 25, 2021, 158 participants were recruited and randomly assigned. Of these, eight (5%) individuals were excluded and 150 participants were allocated to a treatment group (74 in the ENO Breathe group and 76 in the usual care group). Compared with usual care, ENO Breathe was associated with an improvement in MHC score (regression coefficient 2·42 [95% CI 0·03 to 4·80]; p=0·047), but not PHC score (0·60 [–1·33 to 2·52]; p=0·54). VAS for breathlessness (running) favoured ENO Breathe participation (−10·48 [–17·23 to –3·73]; p=0·0026). No other statistically significant between-group differences in secondary outcomes were observed. One minor self-limiting adverse event was reported by a participant in the ENO Breathe group who felt dizzy using a computer for extended periods. Thematic analysis of ENO Breathe participant experience identified three key themes: (1) improvements in symptoms; (2) feeling that the programme was complementary to standard care; and (3) the particular suitability of singing and music to address their needs.

Interpretation. Our findings suggest that an online breathing and wellbeing programme can improve the mental component of HRQoL and elements of breathlessness in people with persisting symptoms after COVID-19. Mind–body and music-based approaches, including practical, enjoyable, symptom-management techniques might have a role supporting recovery.
[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00125-4/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600%2822%2900125-4/fulltext)

**rates and variants**

**title:** Household Secondary Attack Rates of SARS-CoV-2 by Variant and Vaccination Status: An Updated Systematic Review and Meta-analysis

jama network open| 28th april 2022

Question Are viral variants of concern and increased vaccination associated with SARS-CoV-2 household transmission rates?

Findings In this systemic review and meta-analysis of 135 studies with more than 1.3 million participants in 36 countries, household secondary attack rates increased over time and were higher for Omicron (42.7%), Alpha (36.4%), and Delta (29.7%) variants than previously reported estimates (18.9%). Full vaccination reduced susceptibility and infectiousness, but more so for Alpha than Delta and Omicron.

Meaning These findings suggest vaccination for SARS-CoV-2 transcends protection of the individual by conferring indirect protection to other household members, but the degree of protection is seemingly lower for emerging variants.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791601>

**infection control**

**title:** The benefits of large scale covid-19 vaccination

BMJ |27TH april 2022

New evidence confirms that fewer people die in better vaccinated communities

The first covid-19 vaccines were administered under emergency use authorisation in December 2020, just one year into the pandemic, a “miracle” of pharmaceutical innovation that has saved an estimated million lives or more in the US alone.12 The authorisation was given on the basis of safety and efficacy in randomised controlled trials, which found that immunisation with Pfizer-BioNTech and Moderna mRNA vaccines protected a remarkably high percentage (>90%) of recipients from developing symptomatic infection and, to a lesser extent, from asymptomatic infection too. In other words, when tested against the SARS-CoV-2 variants prevailing in 2020 and early 2021, these novel covid-19 vaccines could stop the great majority of infections from causing illness and help to prevent transmission of SARS-CoV-2. But could vaccination prevent infection and illness on a large scale, outside the controlled environment of clinical trials? A linked study by Suthar and colleagues (doi:10.1136/bmj-2021-069317) adds to the evidence that it can, across the US.3

Given the practical challenges of scaling up immunisation programmes—maintaining cold chains, carrying out mass inoculation in busy or makeshift clinics, and accurately reporting both numbers vaccinated and health outcomes—real world vaccine effectiveness is typically less than the efficacy achieved in clinical trials. Following reports that effectiveness has remained high for a variety of outcomes (infection, symptomatic illness, visits to emergency departments, hospital admissions, severe illness, and death) in diverse settings,45678910 Suthar and colleagues have now investigated the impact of covid-19 vaccination, largely with Pfizer and Moderna vaccines, across 2558 counties in 48 US states, covering nearly 80% of the US population. Their evaluation is based on more than 30 million cases of covid-19 and more than 400 000 deaths linked to covid-19, which were reported during the second year of the pandemic, between December 2020 and December 2021.3

They measured effectiveness by comparing reported covid-19 incidence and mortality rates in counties with very low (0-9%), low (10-39%), medium (40-69%), and high (≥70%) percentages of adults (≥18 years) who had received at least one dose of vaccine. During the first half of 2021, when the alpha variant of SARS-CoV-2 was dominant, the covid-19 mortality rate was reduced by 60%, 75%, and 81% in counties with low, medium, and high vaccination coverage, compared with counties that had very low coverage. The corresponding figures for the reduction in case incidence were 57%, 70%, and 80%. The impact on mortality was similar during the second half of 2021 when the delta variant became dominant in the US, with smaller effects on incidence.3

Clearly, counties with higher vaccination coverage had fewer covid-19 cases and deaths per head of population, and the measured effectiveness in counties with high vaccine coverage was reassuringly large. More than this, vaccination had a disproportionately large effect in counties with low and medium coverage. For instance, an incremental increase in coverage of only 20% (from very low to low) and 50% (from very low to medium) led to reductions in mortality of 60% and 75%, respectively.

Suthar and colleagues argue that vaccination benefits whole communities, and indeed it does when coverage is high.3 But they did not seek, and their data do not show, any extra effect of herd immunity, whereby vaccinated people prevented the transmission of infection to others in their communities.11 A more likely explanation for the disproportionately beneficial effect in counties with low and medium coverage is that vaccination campaigns first targeted older people who are at greatest risk of severe illness and death from covid-19. Vaccine rollout in most countries began with older and otherwise vulnerable people and progressively included younger and less vulnerable people. Hong Kong is a notable exception, where high covid-19 death rates in March 2022 were associated with low vaccination rates particularly among older people.12 Unlike Hong Kong, the US has followed the norm: in states that have achieved relatively low vaccination coverage overall, the percentage of older people vaccinated is invariably higher than the population average.13 Suthar and colleagues did not investigate the effect of vaccination by age, but doing this should be possible with existing data available to the US Centers for Disease Control and Prevention.

The findings of this study also make clear that many more lives could have been saved, and will be saved, by encouraging people to keep up to date with vaccination in the face of waning immunity and new SARS-CoV-2 variants and by achieving even higher population coverage. How many lives is a matter for others to explore. Meanwhile, this new study is another confidence booster for covid-19 vaccines.
<https://www.bmj.com/content/377/bmj.o867>

**title:** Comparison of Home Antigen Testing With RT-PCR and Viral Culture During the Course of SARS-CoV-2 Infection

jama INTERNAL MEDICINE| 29TH april 2022

Question How does the diagnostic performance of home antigen tests change during the course of SARS-CoV-2 infection?

Findings In this prospective cohort study of 225 adults and children with reverse transcription–polymerase chain reaction (RT-PCR)–confirmed SARS-CoV-2 infection, antigen test sensitivity was 64% and 84% when compared with same-day RT-PCR and viral culture, respectively. Antigen test sensitivity peaked 4 days after illness onset (77%); a second test 1 to 2 days later showed improved sensitivity (81%-85%).

Meaning The study results suggest that symptomatic individuals with an initial negative home antigen test result for SARS-CoV-2 infection should test again 1 to 2 days later because test sensitivity seems to peak several days after illness onset.
<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2791915>

**title:** Public health impact of covid-19 vaccines in the US: observational study

BMJ | 27th april 2022

Objective To evaluate the impact of vaccine scale-up on population level covid-19 mortality and incidence in the United States. Design Observational study. Setting US county level case surveillance and vaccine administration data reported from 14 December 2020 to 18 December 2021. Participants Residents of 2558 counties from 48 US states.

Main outcome measures The primary outcome was county covid-19 mortality rates (deaths/100 000 population/county week). The secondary outcome was incidence of covid-19 (cases/100 000 population/county week). Incidence rate ratios were used to compare rates across vaccination coverage levels. The impact of a 10% improvement in county vaccination coverage (defined as at least one dose of a covid-19 vaccine among adults ≥18 years of age) was estimated During the eras of alpha and delta variant predominance, the impact of very low (0-9%), low (10-39%), medium (40-69%), and high (≥70%) vaccination coverage levels was compared.

Results In total, 30 643 878 cases of covid-19 and 439 682 deaths associated with covid-19 occurred over 132 791 county weeks. A 10% improvement in vaccination coverage was associated with an 8% (95% confidence interval 8% to 9%) reduction in mortality rates and a 7% (6% to 8%) reduction in incidence. Higher vaccination coverage levels were associated with reduced mortality and incidence rates during the eras of alpha and delta variant predominance.

Conclusions Higher vaccination coverage was associated with lower rates of population level covid-19 mortality and incidence in the US.
<https://www.bmj.com/content/377/bmj-2021-069317>

**title:** COVID-19 Vaccination—Becoming Part of the New Normal

jama |2ND MAY 2022

As the US emerges from the recent Omicron surge of the COVID-19 pandemic following close to a million deaths in the country attributable to COVID-19, many people are hoping that the worst is over.1 Widespread vaccine- and infection-induced immunity, combined with the availability of effective therapeutics, could blunt the effects of future outbreaks. Nonetheless, it is time to accept that the presence of SARS-CoV-2, the virus that causes COVID-19, is the new normal. It will likely circulate globally for the foreseeable future, taking its place alongside other common respiratory viruses such as influenza. And it likely will require similar annual consideration for vaccine composition updates in consultation with the US Food and Drug Administration (FDA) Vaccines and Related Biological Products Advisory Committee (VRBPAC). A recent meeting of the VRBPAC on April 6, 2022, resulted in a lively discussion and agreement on many considerations for planning for upcoming approaches to COVID-19 vaccine strain composition decision-making, development, and recommendations…
<https://jamanetwork.com/journals/jama/fullarticle/2792030>

**title:** The BMJ Interview: WHO chief scientist optimistic for a pan-coronavirus vaccine in two years

BMJ| 26th april 2022

Soumya Swaminathan tells Mun-Keat Looi of her worries about the relaxation of testing for global surveillance and the “two track pandemic”

It’s a challenging time to be a scientist, let alone the first ever chief scientist at the World Health Organization, a relatively new role. Barely nine months into her tenure Soumya Swaminathan was faced with a once in a century global health emergency and an entirely new virus that would change the face of science and medicine dramatically…
<https://www.bmj.com/content/377/bmj.o1003>

**title:** Covid-19: Drug companies urged to share vaccine technology to boost equity and access

BMJ| 28th april 2022

Campaigners including the head of the World Health Organization have urged pharmaceutical companies to share technology and knowledge in order to improve covid-19 vaccine equity and access.

WHO director general Tedros Adhanom Ghebreyesus and representatives from the People’s Vaccine Alliance are presenting shareholder resolutions on behalf of Oxfam at the annual general meetings of Moderna, Pfizer, and Johnson & Johnson.123

Abby Maxman, president of Oxfam America, said, “Moderna, Pfizer, and Johnson & Johnson have prioritised short term profit making over long term sustainability and reputational risks, as well as public health needs. The flawed donation based model has produced vast vaccine inequity, despite the desire, willingness, and ability of countries around the world to produce their own doses for their own citizens.”
<https://www.bmj.com/content/377/bmj.o1086>

**title:** Covid-19: Mix and match booster vaccination approach offers best protection, study reports

BMJ|25TH APRIL 2022

Using a different covid-19 vaccine for the third “booster” dose than was used for the initial two doses provides a higher level of protection, a study has found. Researchers from Chile examined the country’s national covid-19 vaccination programme, including over four million people who received two doses of the CoronaVac (Sinovac) vaccine followed by a booster dose between February and November 2021. Around 47% received the Oxford AstraZeneca vaccine as a booster, while about 49% received the Pfizer BioNTech vaccine and just under 5% received the CoronaVac booster.

The team found that the adjusted vaccine effectiveness for preventing symptomatic covid-19 was highest for the Pfizer booster 96.5% (95% confidence interval 96.2 to 96.7), followed by the AstraZeneca booster 93.2% (95% CI 92.9 to 93.6), and then CoronaVac 78.8% (95% CI 76.8 to 80.6).

The paper, presented at the 2022 European Congress of Clinical Microbiology and Infectious Diseases in Lisbon and published in The Lancet Global Health, reported that when it comes to effectiveness against severe disease and death, however, the AstraZeneca booster provided the most protection…
<https://www.bmj.com/content/377/bmj.o1052>

**title:** How to tackle inequitable access, vaccine hesitancy, and other barriers to achieve high vaccine uptake

bmj| 29th april 2022

World Immunisation Week is an opportune moment to reflect on the importance of vaccination as one of the foundations of a functioning public health system. This year presents a unique set of challenges for the European Region, as several European countries begin settling nearly five million refugees from Ukraine, while countries also plan their next steps to control the covid-19 pandemic.

Interest in covid-19 vaccination is faltering in the WHO European Region; the proportion of the region’s population that is fully vaccinated has only increased by 5% so far in 2022: from 58% in January 2022 to 63% in April 2022.1 The disparity in vaccination uptake between countries in the WHO European Region is glaring: 73% of the total population in high income countries have received their complete dose series while only 37% of the total population in low middle income countries have received the same.1 WHO’s target of 70% uptake in all countries by mid-2022 remains an important aspiration, but it will be almost impossible for several countries in the WHO European Region in view of the current pace of vaccination uptake…
<https://www.bmj.com/content/377/bmj.o1094>

**title:** Covid-19: Policy to discharge vulnerable patients to care homes was irrational, say judges

bmj | 29th april 2022

Government policy that exposed thousands of vulnerable elderly people in England to SARS-CoV-2 in the early months of the pandemic was irrational in failing to advise that asymptomatic patients sent to care homes to free up hospital beds should be isolated for 14 days, two senior judges have ruled.1

The decision that Matt Hancock, then health and social care secretary, operated an unlawful policy gives the lie to Hancock’s claim to have thrown a protective ring around care homes when the pandemic struck. About 20 000 care home residents in England died from covid-19 during the first wave of the pandemic in 2020…
<https://www.bmj.com/content/377/bmj.o1098>

**title** Why is respiratory protective equipment still an issue in the NHS?

BMJ | 27th april 2022

Revised NHS guidance has relaxed infection prevention and control (IPC) requirements for hospitals and GP practices. These authors question why airborne transmission is not more clearly acknowledged and why healthcare workers still do not have access to appropriate personal protective equipment

The World Health Organisation (WHO) and the US Centers for Disease Control and Prevention (CDC) both recognise the airborne transmission of SARS-COV-2, at both short and long range, yet there continue to be delays in implementing respiratory protective equipment across the NHS for staff caring for infectious covid-19 patients. Why?

The evidence on airborne transmission of SARS-CoV-2 is overwhelming, readily available, and expertly communicated. SARS-CoV-2 is an aerosol borne virus which infects hosts by being inhaled and this has long been acknowledged in UK government messaging on ventilation.1

In the first wave of covid-19 in 2020, the lack of appropriate personal protective equipment (PPE) for healthcare staff was blamed on supply and production issues. This excuse could have had some credibility if one was to ignore decades of pandemic planning that ought to have pre-empted such an occurrence. However, two years later and the official line is that there are no supply issues. So why are staff still not being provided with adequate PPE? It has never been clear if the stated insufficiency of supply is because this has been calculated based on guidance for non airborne precautions (except for aerosol generating procedures [AGPs]) which, if altered to more sensibly cover physiologically produced aerosols such as when breathing and talking, would significantly alter the levels of supplies required. Given the formal reassurances, this is not a viable reason particularly in a resource rich country…
<https://www.bmj.com/content/377/bmj.o1082>

**title:** COVID-19 Vaccine Effectiveness in Youth Varies by Age, Variant

jama| 26TH april 2022
Two doses of the BNT162b2 (Pfizer-BioNTech) vaccine were more effective for reducing infections with the Delta variant of SARS-CoV-2 than the Omicron variant, a multi-institution study showed. Adolescents also received greater protection from vaccination than younger age groups. Between July 25, 2021, and February 12, 2022, the study investigators administered weekly SARS-CoV-2 testing to 1364 individuals aged 5 to 15 years regardless of symptoms. They also tested participants when they developed symptoms. Vaccinated and unvaccinated youth participated at sites in Arizona, Florida, Texas, and Utah.

Two vaccine doses were 31% effective against symptomatic or asymptomatic Omicron variant infection among children aged 5 to 11 years and 59% effective among adolescents aged 12 to 15 years. In contrast, 2 doses provided 87% protection against Delta variant infection among adolescents. Still, the authors recommended that all children and adolescents should receive COVID-19 vaccines as recommended, as they reduce the risk of infection even with the Omicron variant.

The study also revealed differences in the variants’ effects among unvaccinated youth. About half of unvaccinated children and adolescents with Omicron infections were asymptomatic compared with 34% of those with Delta variant infections. Omicron symptoms lasted 3.4 fewer days and resulted in fewer missed school days than infections with the Delta variant. Vaccination reduced the time children infected with Omicron spent in bed by about a half-day…
<https://jamanetwork.com/journals/jama/fullarticle/2791394>

**title:** Hyper inflammatory syndrome following COVID-19 mRNA vaccine in children: A national post-authorization pharmacovigilance study

the lancet REGIONAL HEALTH EUROPE | 29TH april 2022

Background. Multisystem inflammatory syndrome in children (MIS-C) is the most severe clinical entity associated with pediatric SARS-CoV-2 infection with a putative role of the spike protein into the immune system activation. Whether COVID-19 mRNA vaccine can induce this complication in children is unknown. We aimed to assess the risk of hyper-inflammatory syndrome following COVID-19 mRNA vaccine in children.

Methods. We conducted a post-authorization national population-based surveillance using the French enhanced pharmacovigilance surveillance system for COVID-19 vaccines. All cases of suspected hyper-inflammatory syndrome following COVID-19 mRNA vaccine in 12–17-year-old children between June 15th, 2021 and January 1st, 2022, were reported. Cases were reviewed according to WHO criteria for MIS-C. The reporting rate of this syndrome was compared to the MIS-C rate per 1,000,000 12–17-year-old children infected by SARS-CoV-2.

Findings. Up to January 2022, 8,113,058 COVID-19 mRNA vaccine doses were administered to 4,079,234 12–17-year-old children. Among them, 12 presented a hyper-inflammatory syndrome with multisystemic involvement. Main clinical features included male predominance (10/12, 83%), cardiac involvement (10/12, 83%), digestive symptoms (10/12, 83%), coagulopathy (7/12, 58%), cytolytic hepatitis (6/12, 50%), and shock (5/12, 42%). 4/12 (33%) required intensive care unit transfer, and 3/12 (25%) hemodynamic support. All cases recovered. In eight cases, no evidence of previous SARS-CoV-2 infection was found. The reporting rate was 1.5 (95%CI [0.8; 2.6]) per 1,000,000 doses injected, i.e. 2.9 (95%CI [1.5; 5.1]) per 1,000,000 12–17-year-old vaccinated children. As a comparison, 113 MIS-C (95%CI [95; 135]) occurred per 1,000,000 12–17-year-old children infected by SARS-CoV-2.

Interpretation. Very few cases of hyper-inflammatory syndrome with multi-organ involvement occurred following COVID-19 mRNA vaccine in 12–17-year-old children. The low reporting rate of this syndrome, compared to the rate of post-SARS-CoV-2 MIS-C in the same age-group, largely supports the vaccination in a context of an important circulation of SARS-CoV-2.
[https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00086-2/fulltext](https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762%2822%2900086-2/fulltext)

**title:** Fourth Dose of BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting

NEW ENGLAND JOURNAL OF MEDICINE| 28TH april 2022

With large waves of infection driven by the B.1.1.529 (omicron) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), alongside evidence of waning immunity after the booster dose of coronavirus disease 2019 (Covid-19) vaccine, several countries have begun giving at-risk persons a fourth vaccine dose.

METHODS To evaluate the early effectiveness of a fourth dose of the BNT162b2 vaccine for the prevention of Covid-19–related outcomes, we analyzed data recorded by the largest health care organization in Israel from January 3 to February 18, 2022. We evaluated the relative effectiveness of a fourth vaccine dose as compared with that of a third dose given at least 4 months earlier among persons 60 years of age or older. We compared outcomes in persons who had received a fourth dose with those in persons who had not, individually matching persons from these two groups with respect to multiple sociodemographic and clinical variables. A sensitivity analysis was performed with the use of parametric Poisson regression.

RESULTS. The primary analysis included 182,122 matched pairs. Relative vaccine effectiveness in days 7 to 30 after the fourth dose was estimated to be 45% (95% confidence interval [CI], 44 to 47) against polymerase-chain-reaction–confirmed SARS-CoV-2 infection, 55% (95% CI, 53 to 58) against symptomatic Covid-19, 68% (95% CI, 59 to 74) against Covid-19–related hospitalization, 62% (95% CI, 50 to 74) against severe Covid-19, and 74% (95% CI, 50 to 90) against Covid-19–related death. The corresponding estimates in days 14 to 30 after the fourth dose were 52% (95% CI, 49 to 54), 61% (95% CI, 58 to 64), 72% (95% CI, 63 to 79), 64% (95% CI, 48 to 77), and 76% (95% CI, 48 to 91). In days 7 to 30 after a fourth vaccine dose, the difference in the absolute risk (three doses vs. four doses) was 180.1 cases per 100,000 persons (95% CI, 142.8 to 211.9) for Covid-19–related hospitalization and 68.8 cases per 100,000 persons (95% CI, 48.5 to 91.9) for severe Covid-19. In sensitivity analyses, estimates of relative effectiveness against documented infection were similar to those in the primary analysis.

CONCLUSIONS. A fourth dose of the BNT162b2 vaccine was effective in reducing the short-term risk of Covid-19–related outcomes among persons who had received a third dose at least 4 months earlier.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2201688>

**title:** Covid-19 Boosters — Where from Here?

new england journals of medicine| 21st april 2022

…People are now confused about what it means to be fully vaccinated. It is easy to understand how this could happen. Arguably, the most disappointing error surrounding the use of Covid-19 vaccines was the labeling of mild illnesses or asymptomatic infections after vaccination as “breakthroughs.” As is true for all mucosal vaccines, the goal is to protect against serious illness — to keep people out of the hospital, intensive care unit, and morgue. The term “breakthrough,” which implies failure, created unrealistic expectations and led to the adoption of a zero-tolerance strategy for this virus. If we are to move from pandemic to endemic, at some point we are going to have to accept that vaccination or natural infection or a combination of the two will not offer long-term protection against mild illness.

In addition, because boosters are not risk-free, we need to clarify which groups most benefit. For example, boys and men between 16 and 29 years of age are at increased risk for myocarditis caused by mRNA vaccines.10 And all age groups are at risk for the theoretical problem of an “original antigenic sin” — a decreased ability to respond to a new immunogen because the immune system has locked onto the original immunogen. An example of this phenomenon can be found in a study of nonhuman primates showing that boosting with an omicron-specific variant did not result in higher titers of omicron-specific neutralizing antibodies than did boosting with the ancestral strain.11 This potential problem could limit our ability to respond to a new variant.

It is now incumbent on the CDC to determine who most benefits from booster dosing and to educate the public about the limits of mucosal vaccines. Otherwise, a zero-tolerance strategy for mild or asymptomatic infection, which can be implemented only with frequent booster doses, will continue to mislead the public about what Covid-19 vaccines can and cannot do.
<https://www.nejm.org/doi/full/10.1056/NEJMe2203329>

**title:** Assessment of Antibody and T-Cell Responses to the SARS-CoV-2 Virus and Omicron Variant in Unvaccinated Individuals Recovered From COVID-19 Infection in Wuhan, China

jama network open| 27TH april 2022

The SARS-CoV-2 Omicron variant, which harbored 32 mutations in spike glycoproteins (S),1 raised concern over the virus escaping from immunity induced by vaccination or natural infection.2,3 However, the full extent to which the Omicron variant evades existing vaccine- or infection-derived antibodies, especially memory T-cell responses, has not been well characterized. In this cohort study, we assessed the antibody and T-cell responses to SARS-CoV-2 Wuhan and Omicron strains in individuals recovered from COVID-19…

…In our cohort, the neutralization efficacy of individuals recovered from Wuhan strain without repeated infection and vaccination against Omicron was lower than the original Wuhan strain and Delta variant. Our data and previously studies suggest that Omicron is resistant to vaccine- and infection-elicited antibody responses,2,3 but elicits T-cell responses similar to other variants.5 Omicron may be less likely to cause severe disease in those who have previously been vaccinated or infected because of T-cell cross-reactivity. A limitation of this study is that the correlations of immune responses in plasma and blood cells with those in respiratory mucosa were not assessed. Continuous surveillance is needed to monitor the incidence of breakthrough infections by Omicron.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791571>

**title:** Association of COVID-19 Vaccination With Risk of COVID-19 Infection, Hospitalization, and Death in Heart Transplant Recipients

jama CARDIOLOGY| 27th april 2022

Question Do COVID-19 vaccines provide protection against severe SARS-CoV-2 infection and death in heart transplant recipients?

Findings In this case-control study, heart transplant recipients from a single center who were vaccinated against SARS-CoV-2 had significantly lower risk of COVID-19 infection, hospitalization, and death with no transplant-related safety concerns.

Meaning Even though the immunogenic response to COVID-19 vaccination is lower in patients who receive a heart transplant, the vaccine appears to be safe and is associated with a lower risk of COVID-19 infection, hospitalization, and death, suggesting it is imperative that all heart transplant recipients obtain the COVID-19 vaccine.
<https://jamanetwork.com/journals/jamacardiology/article-abstract/2791262>

**title:** Incidence of Guillain-Barré Syndrome After COVID-19 Vaccination in the Vaccine Safety Datalink

jamA NETWORK OPEN| 26th april 2022

Question Are COVID-19 vaccines associated with Guillain-Barré syndrome (GBS)?

Findings In this cohort study of surveillance data from the Vaccine Safety Datalink that included 15.1 million doses of COVID-19 vaccines, the unadjusted incidence rate of confirmed GBS in the 1 to 21 days after receiving the Ad.26.COV2.S (Janssen) vaccine was 32.4 per 100 000 person-years, which was significantly higher than the background rate of GBS. The unadjusted incidence rate of confirmed GBS in the 1 to 21 days after mRNA vaccines was 1.3 per 100 000 person-years, which did not differ from the background rate.

Meaning These findings suggest an increased risk of GBS after Ad.26.COV2.S vaccination.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791533>

**title:** Risk of Appendicitis After mRNA COVID-19 Vaccination in a Danish Population

JAMA INTERNAL MEDICINE| 25th april 2022

Appendicitis has been reported as a potential adverse event after immunization with mRNA-based COVID-19 vaccines, based on trial data,1 adverse event report data,2 and observational data.3 We evaluated the risk of appendicitis after receiving an mRNA COVID-19 vaccination and after diagnosis of SARS-CoV-2 infection compared with the risk of appendicitis in unvaccinated individuals..

…In this nationwide study comprising 4 million vaccinated individuals, we found no association between immunization with mRNA-based COVID-19 vaccines and appendicitis. The safety signal was raised when BNT162b2 vaccine trials showed higher numbers of appendicitis cases in vaccinated than placebo groups; the US Food and Drug Administration then listed appendicitis as an adverse effect of special interest.1,4 This suspicion was backed by disproportional reporting of adverse events2 and an Israeli cohort study estimating an excess risk of appendicitis of 5.0 episodes per 100 000 individuals after vaccination.3 However, an interim analysis of US surveillance data found no association.5 Limitations of the study include the nonrandomized observational design, accuracy of register-based identification of appendicitis,6 and inability to detect possible risks beyond the predefined risk interval. Further studies from different settings will be needed to fully eliminate appendicitis as an mRNA COVID-19 vaccination safety concern.
<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2791667>

**title:** Effect of mycophenolate mofetil dose on antibody response following initial SARS-CoV-2 vaccination in patients with systemic sclerosis

THE LANCET RHEUMATOLOGY | 27THapril 2022

An attenuated response to SARS-CoV-2 vaccination has been observed in several immunosuppressed populations. Among patients with rheumatic diseases, the use of lymphocyte depleting therapies, such as mycophenolate mofetil and rituximab, have been associated with reduced rates of seroconversion. Mycophenolate mofetil is the mainstay of immunosuppressant therapy for patients with systemic sclerosis, and is often used to treat skin and lung involvement. Lung disease, specifically, has been associated with increased morbidity and mortality from COVID-19. Given the risk of both poor vaccine response and severe COVID-19 outcomes in this patient population, we sought to identify factors associated with negative antibody response after initial SARS-CoV-2 vaccination in a well characterised cohort of patients with systemic sclerosis.

…In conclusion, 30 (30%) of 100 patients with systemic sclerosis who were tested for anti-SARS-CoV-2 IgG did not show evidence of an antibody response following initial SARS-CoV-2 vaccination. Consistent with previous findings, use of mycophenolate mofetil or rituximab was associated with negative antibody response. To our knowledge, this is the first report to investigate the effects of mycophenolate mofetil dose on anti-SARS-CoV-2 IgG antibody response in patients with systemic sclerosis, with patients on high-dose mycophenolate mofetil the least likely to have detectable antibodies. Although a temporary peri-vaccination hold of mycophenolate mofetil augments humoral response in transplant recipients and in patients with rheumatic diseases, this might not be appropriate for all patients; temporary use of low-dose mycophenolate mofetil might represent an alternative strategy to enhance SARS-CoV-2 vaccine response. Our findings highlight the need for ongoing studies to evaluate additional strategies, such as peri-vaccination modulation of immunosuppression, additional vaccine doses, and consideration of pre-exposure prophylaxis to protect this susceptible patient population.
[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00100-X/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913%2822%2900100-X/fulltext)

**title:** Breakthrough SARS-CoV-2 infections with the delta (B.1.617.2) variant in vaccinated patients with immune-mediated inflammatory diseases using immunosuppressants: a substudy of two prospective cohort studies

THE LANCET RHEUMATOLOGY| 29TH april 2022

Background. Concerns have been raised regarding the risks of SARS-CoV-2 breakthrough infections in vaccinated patients with immune-mediated inflammatory diseases treated with immunosuppressants, but clinical data on breakthrough infections are still scarce. The primary objective of this study was to compare the incidence and severity of SARS-CoV-2 breakthrough infections between patients with immune-mediated inflammatory diseases using immunosuppressants, and controls (patients with immune-mediated inflammatory diseases not taking immunosuppressants and healthy controls) who had received full COVID-19 vaccinations. The secondary objective was to explore determinants of breakthrough infections of the delta (B.1.617.2) variant of SARS-CoV-2, including humoral immune responses after vaccination.

…The incidence and severity of SARS-CoV-2 breakthrough infections in patients with immune-mediated inflammatory diseases on immunosuppressants was similar to that in controls. However, caution might still be warranted for those on anti-CD20 therapy and those with traditional risk factors.
[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00102-3/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913%2822%2900102-3/fulltext)

**title:** Immunosuppression and SARS-CoV-2 breakthrough infections

THE LANCET RHEUMATOLOGY | 29th april 2022

…Although there were some signals for breakthrough infection in specific patient groups (eg, seronegative status and some comorbidities), the findings of Boekel and colleagues are reassuring to patients who are immunosuppressed. After vaccination, overall rates and clinical severity of breakthrough infections among patients with immune-mediated inflammatory diseases was similar to among healthy controls. How subsequent variants, such as omicron (B.1.1.529) that might confer reduced vaccine effectiveness, will affect infection rates remains unknown. Patients with immune-mediated diseases who are immunosuppressed might have accelerated waning immunity, placing them at risk over time after vaccine receipt. Therefore, quantifying the effect of additional vaccine doses on breakthrough infection with contemporary circulating variants is needed. Finally, although the findings here offer some evidence that humoral responses confer clinical protection, the specific threshold that offers protection remains unclear. Those with absent humoral responses remain at risk for breakthrough infection, but we continue to caution clinicians to not overinterpret anti-spike antibody levels as a surrogate of protection at the individual level.
[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00127-8/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913%2822%2900127-8/fulltext)

**title:** How repeated influenza vaccination effects might apply to COVID-19 vaccines

THE LANCET RESPIRATORY MEDICINE| 28th april 2022

Many of the current questions on the public health and research aspects of the future of COVID-19 vaccines and vaccine strategies have been topics of research and debate in the influenza vaccine literature for decades. Here, we describe how the lessons learned from the study of repeated influenza vaccinations might apply to the evaluation of COVID-19 vaccines, and the prospect of future seasonal or periodic booster vaccinations…
[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00162-X/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600%2822%2900162-X/fulltext)

**title:** Association of Large Financial Incentives With COVID-19 Vaccination Uptake Among Employees of a Large Private Company [RESEARCH LETTER]

jama open network | 29th april 2022

...In summary, this prospective, school class-based study provides evidence of higher transmission of
Without a federal mandate,1 motivating employees to receive COVID-19 vaccination is a challenge. For influenza vaccination, Nowalk et al2 found that a small ($5) financial incentive increased uptake by 3.4 percentage points in a workplace-based program. However, financial incentives to increase COVID-19 vaccination uptake have mixed outcomes. Campos-Mercade et al3 found that a moderate ($24) cash incentive increased COVID-19 vaccine uptake by 4.2 percentage points, whereas Wong et al4 found that $25 was associated with slower decline of vaccination uptake. Acharya and Dhakal5 found that large but uncertain incentives (lottery programs) across 11 states had mixed success.

 On August 6, 2021, a large medical device manufacturer announced a vaccination incentive program for US-based employees. The program required that all employees watch and acknowledge online educational information. Employees were also encouraged to report their vaccination status. Those fully vaccinated for COVID-19 by September 30, 2021, would receive a $1000 incentive if able to show proof of vaccination. The incentive was paid in October 2021.

…Our results found that a workplace-based large ($1000) guaranteed financial incentive was associated with increased COVID-19 vaccine uptake. Limitations of the study include absence of a control group, being limited to a single company, and possible confounding with full approval of the Pfizer vaccine by the FDA on August 23, 2021.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791735>

**HEALTH MANGEMENT & recovery**

**title:** The Pandemic Determinants of Health [opinion]

JAMA | 29th april 2022

…I remain fulfilled in my work as a primary care physician and am honored to be a part of each patient’s life and journey in health, but increasingly over the past 2 years each clinic session seems filled with tragedy on an unprecedented scale. Prepandemic, we had an interminable list of things to accomplish each visit. Just as our patients’ days and capacities have not extended to accommodate the increased load neither has our allotted time to care for them, and we are tasked to address more and more pandemic determinants of health. I wish I could wave a magic wand and alleviate their pain and suffering or at least bring it down to a level where they might have the mental space to make or keep their health and well-being a priority.

 I offer what I can, a safe space to share openly about how they are doing, followed by commendations to highlight all they have managed to accomplish or maintain during these extraordinary times. At the end of the visit, I carry a simultaneously empty yet full cup, and the patients are sent back into this uncertain world to care for themselves.
<https://jamanetwork.com/journals/jama/fullarticle/2791952>

**title:** Outcomes of In-Person and Telehealth Ambulatory Encounters During COVID-19 Within a Large Commercially Insured Cohort [us]

JAMA NETWORK OPEN | 26th april 2022

Question What is the association of telehealth vs in-person encounters with outcomes of care during the COVID-19 pandemic in the US?

Findings In this cohort study of 40.7 million US commercially insured adults with acute clinical conditions, those with an initial telehealth encounter, compared with an in-person encounter, had higher odds for any follow-up encounter, an emergency department encounter, and in-patient admissions. For people with chronic conditions, the odds were lower for those with an initial telehealth encounter.

Meaning The contrasting patterns of follow-up care among members receiving telehealth for acute and chronic conditions have implications for health services during and after the COVID-19 pandemic.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791531>

**public health & health inequalities**

**title:** The COVID-19 Pandemic Rages on for People Who Are Immunocompromised

JAMA NETWORK OPEN | 27TH april 2022

Janet Handal, who has taken immunosuppressive drugs since her 2010 kidney transplant, hasn’t exactly been impressed by public health messaging about COVID-19. “The CDC [US Centers for Disease Control and Prevention] has done a bad job with managing the immunocompromised from the get-go,” the 71-year-old Handal, a New York City resident, said in an interview. Take the CDC’s decision in May 2021 to announce that fully vaccinated individuals no longer needed to wear face masks or practice social distancing in most places.

In a video in which she discussed the policy change, CDC Director Rochelle Walensky, MD, MPH, did mention once that people who were immunocompromised should check with their physician before doffing their masks, but she repeatedly said that everyone who was fully vaccinated could do so.

Handal, who created a Facebook group about vaccines and organ transplants that has more than 2000 members and founded the Transplant Recipients and Immunocompromised Patient Advocacy Group, said she knows at least 1 fully vaccinated individual with a compromised immune system who listened to the CDC, took off their mask, contracted COVID-19, and died…
<https://jamanetwork.com/journals/jama/fullarticle/2791868>

**title:** Battling Falsehoods in the COVID-19 Pandemic

JAMA health forum | 28TH april 2022

“Hello, doctor, I was calling to find out if the new variant is connected to the world economic forum and Charles Schwab and microchipping the public in order to tie it into the new banking system?” I was live on C-SPAN’s Washington Journal, where I had been invited in early April 2022 to talk about the public health podcast from the Bloomberg School of Public Health at Johns Hopkins University and answer calls from the public about the pandemic. In the split second after Susan from Los Angeles, California, posed her question to me, the word “infodemic” popped into my head. The World Health Organization defines this term as “too much information including false or misleading information in digital and physical environments during a disease outbreak,” and the US Surgeon General considers it a “serious threat to public health.”

The symptoms of the infodemic may seem bizarre but the consequences are deadly serious. Confusion keeps people from taking steps to protect themselves, falsehoods reduce interest in vaccination, and lies about public officials undermine trust in public health. The Kaiser Family Foundation has found that nearly 4 in 5 adults either believe or are unsure of at least 1 false statement about COVID-19. One-third of adults believe or are unsure of at least 4 false statements. Researchers have estimated that misinformation has stopped between 2 million and 12 million people from being vaccinated. While fielding questions from Susan from Los Angeles and other callers, I gained a deeper appreciation for why the US ranks 62nd of 179 countries or more in global COVID-19 vaccination rates despite having the earliest access to the most effective vaccines in the world.

 What is happening? A recent report from the Johns Hopkins University Center for Health Security found that falsehoods are spreading so rapidly that they are “impossible to counter in real time through official channels.” A recent review in Nature Medicine noted that people are more likely to believe claims that they hear again and again because “the more a claim is repeated, the more familiar it becomes and the easier it is to process.”…
<https://jamanetwork.com/journals/jama/fullarticle/2791868>

**title:** White Individuals Experience Less COVID-19–Related Discrimination

JAMA | 26TH april 2022

Compared with White individuals, all other major racial and ethnic groups in the US experience more COVID-19 discrimination, according to a study coauthored by researchers from the National Institute on Minority Health and Health Disparities. Respondents who identified as Asian, irrespective of national origin, and American Indian or Alaska Native individuals were most likely to experience such discrimination. The findings also suggest that COVID-19 discrimination against Asian individuals has increased over the course of the pandemic.

 The authors analyzed YouGov survey data collected between December 2020 and February 2021 from 5500 US adults. Respondents answered questions posed in English or Spanish about their exposure to COVID-19–related discrimination. Experiencing discriminatory behavior was defined as hearing racist comments, being harassed or threatened, or being called names or insulted—specifically because someone thought the respondent had COVID-19.
<https://jamanetwork.com/journals/jama/fullarticle/2791428>

**mental health**

**title:** Stress-Related Disorders of Family Members of Patients Admitted to the Intensive Care Unit With COVID-19

JAMA internal medicine | 25TH april 2022

Question What are the psychological sequelae of having a family member with COVID-19 admitted to the intensive care unit (ICU)?

Findings In this prospective, mixed-methods cohort study of 330 family members of patients admitted to the ICU with COVID-19, family members had significant symptoms of posttraumatic stress disorder (PTSD) 3 months after the patients’ admission to the ICU; higher PTSD symptoms scores were significantly associated with Hispanic ethnicity, female gender, and previous medication use for a psychiatric condition. Family members with higher scores more commonly described feelings of distrust and concern about the need to take clinicians’ information at face value without being present to see for themselves.

Meaning Having a family member with COVID-19 in the ICU was associated with a high prevalence of symptoms of PTSD, and identified associations may guide future interventions.
<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2791664>

**title:** Evaluation of Suicides Among US Adolescents During the COVID-19 Pandemic

JAMA pediatrics | 25TH april 2022

In 2021, the American Academy of Pediatrics declared a state of emergency regarding child and adolescent mental health.1 During the COVID-19 pandemic, US adolescents have been affected by the widespread loss of primary caregivers. Suicide-risk screenings have yielded higher positive rates than during the prepandemic period2; thus, we sought to measure suicide-related mortality in this population.

…Discussion. Proportion of suicides among adolescents has shifted markedly and heterogeneously across the 14 participating states. Although the study was limited to states with available data, this 14-state cohort included representation from all 10 Department of Health and Human Services regions and comprised 32% of all US residents (33% adolescents). Future research is needed to expand this analysis to the remaining US states. The format of data available from each state varies greatly, but any existing aberrations are unlikely to change the directionality of the findings because of standardization of International Classification of Diseases coding across states.

In accordance with previous work on excess mortality during the pandemic,4 we treated the full year of 2020 as the pandemic period. Although previous studies reported that suicide-related deaths in the broader population decreased during the pandemic,5 we found that adolescents have not experienced the same patterns as adults in the participating 14 states in the same period; specifically, suicides among adults 35 years or older have followed a downward pattern,5 although there is undoubtedly variation across geographic areas and subpopulations. Stratification by age group and geography will be necessary to expose these heterogeneities in mental health outcomes associated with the pandemic. Moreover, given recent evidence that pandemic-period suicidality may be differentially affected by race and ethnicity, especially among youth, future work is needed to capture variability across ethnoracial subpopulations. These findings highlight the importance of alleviating the downstream consequences of the pandemic for adolescent well-being. Examples of interventions that may address shifting suicidality among young people in the US include expanding bereavement counseling to cope with the loss of caregivers and implementing more readily available suicide risk assessment solutions.
<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2791544>

**title:** Data Divide—Disentangling the Role of the COVID-19 Pandemic on Child Mental Health and Well-being

jama pediatrics | 25th april 2022

As research regarding the role of the COVID-19 pandemic on the mental health and well-being of children and youth mounts, an apparent disconnect between certain study findings has emerged. On the one hand, numerous studies confirm increases in depression, anxiety, and eating disorders among youth since the onset of the pandemic.1,2 On the other hand, stable or declining rates of substance use, and to some extent, self-harm and suicidality, have been reported.3,4 We have also seen a disconnect between the magnitude of psychological distress reported among youth during the pandemic and the frequency with which they have presented to the hospital. For example, a recent meta-analysis over the first year of the pandemic found that 1 in 4 children (25%) now experience clinically significant depressive symptoms and 1 in 5 children (20%) experience clinically significant anxiety symptoms.1 However, some studies using administrative health data have observed no increases in hospital presentations for intentional youth self-harm or suicidality.3 How can these seemingly disparate sets of findings coexist?
<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2791540>

**international perspectives**

**title:** Covid-19: China installs fences and alarms in Shanghai in effort to curb cases

bmj | 27th april 2022

The Chinese government has introduced unprecedented public health measures in the city of Shanghai in an effort to curb an outbreak of covid-19 and is reportedly considering locking down Beijing if infections continue to climb in the capital.

Residents of Shanghai have been locked down for a month but woke up to unexpected restrictions late last week. Local authorities erected two metre high fences outside the residences of some communities with a confirmed covid-19 infection to prevent residents from going outside.1

Electronic alarms have also been installed on the doors of residences with a confirmed covid-19 infection. Some residents have been evacuated so that their homes can be disinfected.

The measures come amid signs that China’s strict covid-19 strategy, which has been largely successful in keeping infections close to zero during the pandemic, may not work against the more infectious omicron variant…
<https://www.bmj.com/content/377/bmj.o1076>

**title:** Report Says US Health Agencies Need Better Processes to Address Political Interference

JAMA | 26th april 2022

Four US health agencies lack or have inadequate procedures for defining political interference in scientific decision-making or detailing how such meddling should be reported and addressed, according to a new report from the US Government Accountability Office (GAO).

Agency employees told GAO investigators that they had observed incidents they perceived as political meddling but did not report them because they feared retaliation or believed that agency leadership was already aware of the interference.

The GAO, described as a “congressional watchdog” because of its role in providing auditing, evaluation, and investigative services for the US Congress, reviewed how the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the Office of the Assistant Secretary for Preparedness and Response (ASPR) handle political meddling in their work…
<https://jamanetwork.com/journals/jama-health-forum/fullarticle/2791814>

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