COVID-19 weekly update

1st April 2022

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**clinical management**

**Title:** Use covid age to assess risk for vulnerability to covid-19

bmj| 29th february 2022

In England, all government restrictions on covid-19, including the legal requirement to self-isolate, ended in February. Shemtob and colleagues highlight the importance of continuing risk assessment, a duty under health and safety law. Assessment of risk for vulnerability to covid-19 takes into account comorbid conditions, immunisation, past infection, and viral prevalence. Employers, occupational health practitioners, and treating clinicians have been using a variety of assessment tools over the past two years, most of which have not been based on evidence or have attempted to integrate objective evidence with consensus. The result has been confusion and often bad advice. The “clinically extremely vulnerable” list has been the main source of consensus guidance, but it is not evidence based and is fundamentally flawed, failing to acknowledge the effect of age and the combined effect of risk factors. The government’s own QCovid3 tool demonstrated this in the summer of 2020 yet no action was taken to remove the shielding list or warn the public. Any risk assessment tool incorporating the shielding list is also inevitably flawed.

We recommend using covid age as a simple, evidence based tool that is readily accessible. The team producing the tool have been regularly updating the guidelines as new data become available. For the one and a half million people advised to shield inappropriately, the tool can help to reassure them.
<https://www.bmj.com/content/376/bmj.o826.full>

**Title:** Covid-19: Researchers call for routine flu testing of hospital inpatients with SARS-CoV-2 infection

BMJ| 28th march 2022

All hospital inpatients with covid-19 should be routinely tested for influenza viruses, as those who are co-infected have much worse outcomes, researchers have said. The largest study to date of people with covid-19 undergoing additional testing for other respiratory viruses found that patients in hospital infected with both influenza and SARS-CoV-2 were put on a mechanical ventilator four times as often and were twice as likely to die as patients with only SARS-CoV-2 infection.

The research, by the International Severe Acute Respiratory and Emerging Infection Consortium, included data from 212 466 adults with SARS-CoV-2 infection who were admitted to hospital in the UK between 6 February 2020 and 8 December 2021. Viral co-infection was detected in 583 of 6965 patients with SARS-CoV-2. Of these, 227 patients had influenza viruses, 220 patients had respiratory syncytial virus, and 136 patients had adenoviruses.

The researchers carried out a weighted analysis to take into account that patients who were tested for more than one respiratory virus were typically sicker than patients who were only tested for SARS-CoV-2. They found that, compared with SARS-CoV-2 infection alone, patients who also had influenza were more likely to need invasive mechanical ventilation (odds ratio 4.14, 95% confidence interval 2.00 to 8.49) and to die (2.35, 1.07 to 5.12). Co-infection with respiratory syncytial virus or adenovirus did not significantly increase the risk of ventilation or death…
<https://www.bmj.com/content/376/bmj.o809>

**Title:** Helen Salisbury: Are antivirals a covid-19 game changer?

BMJ| 29th march 2022

…At the surgery, we’re doing our best to support the patients we know about by monitoring the more vulnerable ones with home oxygen saturation meters, while making regular telephone calls to check in. Many patients have heard about the antibody treatments and antiviral medicines that are effective at reducing the need for hospital care,1 and they’re naturally keen to access them. In theory, people who fit the new definition of “clinically extremely vulnerable” have been contacted by the relevant hospital department and supplied with PCR tests to use as soon as they have symptoms, as well as information on how to access those treatments if the result is positive.

Not surprisingly, confusion abounds. People who should be on the list may have been missed, and some people who were previously classed as clinically extremely vulnerable are puzzled when they don’t qualify for the new treatments now that the definition has changed. All of which leads to a lot of phone calls from patients to GPs and a backlog at the hospital, where some poor immunologist now has to sift through hundreds of incoming calls and emails and make decisions.

Locally, the current turnaround time for those decisions is 48 hours. Given that these drugs are most effective in the first two days of infection—and considered ineffective if given after more than five days—the likelihood is that if you’re not already on the list, and pre-armed with a test, your chance of accessing the medicine in time for it to make a real difference is negligible.

When these antiviral medicines were first unveiled there was a big fanfare, with the term “game changer” appearing in numerous headlines. The reality so far has been more modest. For the individual patients who are eligible these medicines may indeed be life saving, but unless easier access to both testing and tablets is proposed, it seems likely that their impact will continue to be limited…
<https://www.bmj.com/content/376/bmj.o810>

**title:** Ruxolitinib in addition to standard of care for the treatment of patients admitted to hospital with COVID-19 (RUXCOVID): a randomised, double-blind, placebo-controlled, phase 3 trial

the lancet rheumatology| 29th march 2022

In October 2021, the US Food and Drug Administration granted emergency use authorization for the
COVID-19 is associated with acute respiratory distress and cytokine release syndrome. The Janus kinase (JAK)1/JAK2 inhibitor ruxolitinib reduces inflammatory cytokine concentrations in disorders characterised by cytokine dysregulation, including graft-versus-host disease, myelofibrosis, and secondary hemophagocytic lymphohistiocytosis. We assessed whether treatment with the JAK1/JAK2 inhibitor ruxolitinib would be beneficial in patients with COVID-19 admitted to hospital.

Methods. RUXCOVID was an international, randomised, double-blind, phase 3 trial of ruxolitinib plus standard of care versus placebo plus standard of care in patients with COVID-19. Patients who were hospitalised but not on mechanical ventilation or in the intensive care unit [ICU] were randomly assigned (2:1) to oral ruxolitinib 5 mg twice per day or placebo for 14 days (14 additional days were allowed if no improvement). The primary endpoint was a composite of death, respiratory failure (invasive ventilation), or ICU care by day 29, analysed by logistic regression including region, treatment, baseline clinical status, age, and sex as covariates. This trial is registered with ClinicalTrials.gov, NCT04362137.

Findings. Between May 4 and Sept 19, 2020, 432 patients were randomly assigned to ruxolitinib (n=287) or placebo (n=145) plus standard of care; the mean age was 56·5 years (SD 13·3), 197 (46%) were female, and 235 (54%) were male. The primary objective was not met: the composite endpoint occurred in 34 (12%) of 284 ruxolitinib-treated patients versus 17 (12%) of 144 placebo-treated patients (odds ratio 0·91, 95% CI 0·48–1·73; p=0·77). By day 29, nine (3%) of 286 ruxolitinib-treated patients had died compared with three (2%) of 145 placebo-treated patients; 22 (8%) of 286 ruxolitinib-treated patients had received invasive ventilation compared with ten (7%) of 145 placebo-treated patients; and 30 (11%) of 284 ruxolitinib-treated patients had received ICU care compared with 17 (12%) of 144 placebo-treated patients. In an exploratory analysis, median time to recovery was 1 day faster with ruxolitinib versus placebo (8 days vs 9 days; hazard ratio 1·10, 95% CI 0·89–1·36). Adverse events included headache (23 [8%] of 281 on ruxolitinib vs 11 [8%] of 143 on placebo) and diarrhoea (21 [7%] vs 12 [8%]).

Interpretation. Ruxolitinib 5 mg twice per day showed no benefit in the overall study population. A larger sample is required to determine the clinical importance of trends for increased efficacy in patient subgroups.
[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00044-3/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913%2822%2900044-3/fulltext)

**title:** Risk of hospitalisation and death in children with SARS-CoV-2 delta (B.1.612.2) infection

the lancet child & Adolescent health| 29th march 2022

…The low hospitalisation rates in children with alpha and delta variant infections confirmed by genotyping should reassure parents, clinicians, and policy makers of the low risk of severe COVID-19 in children. Delta variant infections have, however, resulted in more childhood hospitalisations than alpha. Further studies are needed to distinguish between incidental infections and hospitalisation for severe COVID-19, especially in children, where the former is common, and the latter is rare. COVID-19 vaccines have been shown to reduce the risk of hospitalisation and severe COVID-19 in adults and adolescents. Similar studies are needed to assess the risk of severe COVID-19 in children infected with more recent and emerging variants.
[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(22)00096-7/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642%2822%2900096-7/fulltext)

**title:** Autoantibodies against interleukin-1 receptor antagonist in multisystem inflammatory syndrome in children: a multicentre, retrospective, cohort study

the lancet rheumatology | 29th march 2022

Multisystem inflammatory syndrome in children (MIS-C) is a rare but serious complication of infection with SARS-CoV-2. A possible involvement of pathogenetically relevant autoantibodies has been discussed. Recently, neutralising autoantibodies against inflammatory receptor antagonists progranulin and interleukin-1 receptor antagonist (IL-1Ra) were found in adult patients with critical COVID-19. The aim of this study was to investigate the role of such autoantibodies in MIS-C...

…Anti-IL-1Ra autoantibodies were observed in a high proportion of patients with MIS-C and were specific to these patients. Generation of these autoantibodies might be triggered by an atypical, hyperphosphorylated isoform of IL-1Ra. These autoantibodies impair IL-1Ra bioactivity and might thus contribute to increased IL-1β-signalling in MIS-C.
[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00064-9/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913%2822%2900064-9/fulltext)

**title:** Availability of oral antivirals against SARS-CoV-2 infection and the requirement for an ethical prescribing approach

THE LANCET infectious diseases| 29TH march 2022

The first two oral antivirals, molnupiravir and nirmatrelvir–ritonavir, are now becoming available in many countries. These medicines will be indicated to treat mild-to-moderate COVID-19 in non-hospitalised patients who are at high risk of progressing to severe COVID-19. These antivirals should be prescribed within 5 days of symptom onset, and after SARS-CoV-2 infection has been confirmed. However, the availability of these antivirals will be scarce for some time due to manufacturing constraints. Each country should establish a policy on the conditions under which these antivirals can be prescribed. Such a policy should be based on the fulfilment of five ethical elements: transparency, relevance, appeals, enforcement, and fairness. Following the principles of distributive justice, molnupiravir and nirmatrelvir–ritonavir should be prescribed according to a hierarchy of predicted efficacy, ideally on the basis of an evidence-based scoring system. The placebo-controlled randomised trials that supported the temporary authorisation of these two antivirals were conducted in unvaccinated patients with COVID-19, so an evidence-based prescription practice would only use these drugs for unvaccinated patients until further data become available. However, in the countries that authorised these antivirals in 2021 (the UK and the USA), both vaccinated and unvaccinated patients meeting particular requirements have access to these antivirals. Due to the complexity of prioritisation, national health authorities should start issuing their draft policies as soon as possible and these policies should be regularly updated. The effectiveness of these antivirals against the omicron variant of SARS-CoV-2 must be urgently assessed. Once implemented, molnupiravir and nirmatrelvir–ritonavir must show their effectiveness and safety in the real world, and health systems must be adequately adapted for the correct use of these antivirals.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00119-0/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900119-0/fulltext)

**title:** No perfect therapy for the imperfect COVID-19 cytokine storm

THE LANCET rheumatology| 29th march 2022

Since the emergence of the COVID-19 pandemic, confirmed cases and cumulative deaths have been
More than 2 years into the pandemic, almost 6 million people have died from COVID-19 worldwide. Many people who succumbed to the virus had cytokine storm syndrome, a dysregulated immune response to the pathogen. Progress toward treating COVID-19 has been substantial on several fronts, including rapidly developed safe and effective vaccines, and various antiviral therapies (eg, monoclonal antibody therapies, protease inhibitors, and nucleoside analogues). Antiviral approaches are particularly effective early during infection, but cytokine targeted therapies have shown benefit during later stages of illness, when hyperinflammation is present. The most promising treatment for COVID-19 hyperinflammation is glucocorticoids when given to patients admitted to hospital with COVID-19 who require oxygen. Nonetheless, this broadly immunosuppressive approach has not been that effective. Targeting individual pro-inflammatory cytokines (eg, interleukin [IL]-1 and IL-6) has shown some survival benefit but, again, the effect has been rather underwhelming.

Somewhere in between these two approaches, Janus kinase (JAK) inhibitors disrupt signalling downstream from receptors that bind multiple cytokines. Different small molecule JAK inhibitors target different kinases associated with various cytokine receptors, and ruxolitinib preferentially targets JAK1 and JAK2, which signal downstream of numerous pro-inflammatory cytokines, including IL-6 and interferon-γ.

 In The Lancet Rheumatology, MeiLan Han and colleagues report results from a randomised, double-blind, placebo-controlled trial of ruxolitinib to treat patients with COVID-19 (RUXCOVID). In the RUXCOVID trial, 432 patients with COVID-19 were randomly assigned (2:1) to ruxolitinib (5 mg twice daily for 2 weeks) plus standard of care or placebo plus standard of care. The primary endpoint was a composite of death and requirement for invasive ventilation or intensive care by day 29. 34 (12%) of 284 ruxolitinib-treated patients and 17 (12%) of 144 placebo-treated patients met the composite endpoint (odds ratio 0·91, 95% CI 0·48–1·73; p=0·77), but the median time to recovery was 1 day faster in the ruxolitinib group, although this difference was not statistically significant (hazard ratio 1·10, 95% CI 0·89–1·36). Han and colleagues concluded that ruxolitinib showed no benefit for the overall study population and that a larger clinical trial is necessary to show potential benefit in subgroups of patients with COVID-19 who showed potential improvement with ruxolitinib.

The RUXCOVID trial is another failed attempt to treat the hyperinflammation associated with COVID-19 with immunomodulatory therapy. These results differ from a trial that showed some COVID-19 survival benefit for another JAK1/2 inhibitor, baricitinib, when used in combination with the antiviral remdesivir. Less than 8% of patients with COVID-19 in the RUXCOVID trial received remdesivir, which might have contributed to this disparity in findings. Additionally, only slightly more than half of the patients in the RUXCOVID study received dexamethasone, which is now standard of care for patients admitted to hospital with COVID-19, and might allow for anti-cytokine approaches to be beneficial. Another JAK inhibitor, tofacitinib, showed a COVID-19 survival benefit in conjunction with standard of care (89% of patients received glucocorticoids). Thus, JAK inhibitors, which inhibit signalling from multiple cytokines and are intermediate between glucocorticoid-induced broad immunosuppression and targeted cytokine approaches, appear to have a role in treating patients admitted to hospital with COVID-19.

So, why is that some cytokine inhibitors, including different JAK inhibitors, show benefit for patients admitted to hospital with COVID-19, and others do not? Trial design, including patient selection, different standard of care regimens, and timing of therapies, could be critical. The lack of benefit of ruxolitinib for patients with COVID-19 in the RUXCOVID trial is somewhat surprising, given the ability of ruxolitinib to benefit a wide variety of patients with cytokine storm syndrome. Therefore, the combination of glucocorticoids and ruxolitinib could be crucial to optimise therapy for patients with cytokine storm syndrome. Moreover, as the optimal inflammatory features of COVID-19 were relatively unknown at the time of the RUXCOVID trial, patient selection did not include features such as high C-reactive protein, hyper-ferritinaemia, or elevated pro-inflammatory cytokine concentrations, but rather relied strictly on clinical criteria. Patients with COVID-19 with hyperinflammatory states are more likely to benefit from anti-cytokine therapies. Interestingly, ruxolitinib lowered IL-2RA levels, a marker of hyperinflammation, in the RUXCOVID trial. Although some laboratory markers (eg, IL-2RA, ferritin, D-dimers, C-reactive protein, and IL-6) of more standard varieties of cytokine storm syndrome are elevated in patients with COVID-19, the degree of elevation is often modest, and only subsets of patients with COVID-19 meet traditional criteria for cytokine storm syndrome. Unsurprisingly, established treatment approaches used for cytokine storm syndrome before the SARS-CoV-2 pandemic are notably less effective in treating the imperfect cytokine storm associated with COVID-19. Although there has been clear progress in dampening the cytokine storm associated with COVID-19, prevention of developing COVID-19 through highly effective and safe vaccines remains a priority.
[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00068-6/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913%2822%2900068-6/fulltext)

**title:** IL-1 receptor antagonist, MIS-C, and the peculiar autoimmunity of SARS-CoV-2

the lancet rheumatology | 29th march 2022

In a report in The Lancet Rheumatology, Jochen Pfeifer and colleagues identified high-titre autoantibodies against interleukin-1 receptor antagonist (IL-1Ra) in sera from 13 (62%) of 21 children with MIS-C (age 0–18 years; 19 sampled before receiving IVIG). Anti-IL-1Ra autoantibodies were absent in an array of control participants (healthy children, children with suspected growth retardation [non-inflammatory group], children with mild or asymptomatic COVID-19, children with Kawasaki disease, and children with quiescent systemic juvenile idiopathic arthritis). An unrelated antibody (against Clostridium tetanus toxin) was not elevated in patients with MIS-C versus the control groups, suggesting their findings are not simply the result of non-specific polyclonal stimulation of plasmacytes. In a preprint paper, the same researchers reported anti-IL-1Ra autoantibodies in about 50% of adults with severe or critical COVID-19. Given the increasing evidence of a link between excess IL-1 and Kawasaki disease-like phenotypes, we are intrigued by the possibility that such autoantibodies could be contributing to MIS-C. Supporting this hypothesis, free IL-1Ra protein concentrations were lower in patients with MIS-C who were positive for anti-IL-1Ra autoantibodies, versus those who were negative for autoantibodies, or those with Kawasaki disease or quiescent systemic juvenile idiopathic arthritis. Western blots revealed antibody-IL-1Ra complexes, and reporter assays suggested neutralisation of IL-1Ra activity by autoantibody-containing plasma. Decreased autoantibody titres during longitudinal follow-up of two patients with MIS-C suggested that these autoantibodies were transient. The authors also offer a potential mechanism of IL-1Ra-specific autoimmunity: they identified a hyperphosphorylated form of IL-1Ra in the patients with MIS-C who were positive for anti-IL-1Ra autoantibodies, but not in the control groups or autoantibody-negative patients with MIS-C. Similarly, rises and falls in hyperphosphorylated IL-1Ra preceded corresponding rises and falls in anti-IL-1Ra autoantibodies in their adult COVID-19 cohort and in one of the patients with MIS-C.

These observations are provocative, placing IL-1 signalling downstream of SARS-CoV-2 infection but upstream of hyperinflammation in patients with MIS-C. Yet, this preliminary study has several limitations, including a small number of participants, few longitudinal samples, and incomplete mechanistic evaluation. As such, these findings should neither affect clinical decision making, nor favour an expanded front-line use of anakinra (recombinant IL-1Ra) in patients with MIS-C, particularly given the complete response of most patients to IVIG and glucocorticoids. However, if generalisable, these results inspire important questions (panel). The range and scope of such questions are a testament to the potential novelty and aetiological importance of this study. The apparently unique association of hyperphosphorylated IL-1Ra and neutralising autoantibodies after SARS-CoV-2 infection might launch a new line of study with great translational potential. In the interim, we can thank the unprecedented scientific response to SARS-CoV-2 and its related morbidities for another insight into the host–pathogen autoimmunity problem.
[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00090-X/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913%2822%2900090-X/fulltext)

**title:** Effect of Early Treatment with Ivermectin among Patients with Covid-19

NEJM | 30th march 2022

The B.1.1.529 (omicron) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
The efficacy of ivermectin in preventing hospitalization or extended observation in an emergency setting among outpatients with acutely symptomatic coronavirus disease 2019 (Covid-19), the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is unclear. Methods: We conducted a double-blind, randomized, placebo-controlled, adaptive platform trial involving symptomatic SARS-CoV-2–positive adults recruited from 12 public health clinics in Brazil…

…Treatment with ivermectin did not result in a lower incidence of medical admission to a hospital due to progression of Covid-19 or of prolonged emergency department observation among outpatients with an early diagnosis of Covid-19.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2115869?query=featured_coronavirus>

**title:** Early Outpatient Treatment for Covid-19 with Convalescent Plasma

NEJM | 30th march 2022

The B.1.1.529 (omicron) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
Polyclonal convalescent plasma may be obtained from donors who have recovered from coronavirus disease 2019 (Covid-19). The efficacy of this plasma in preventing serious complications in outpatients with recent-onset Covid-19 is uncertain.

Methods. In this multicenter, double-blind, randomized, controlled trial, we evaluated the efficacy and safety of Covid-19 convalescent plasma, as compared with control plasma, in symptomatic adults (≥18 years of age) who had tested positive for severe acute respiratory syndrome coronavirus 2, regardless of their risk factors for disease progression or vaccination status. Participants were enrolled within 8 days after symptom onset and received a transfusion within 1 day after randomization. The primary outcome was Covid-19–related hospitalization within 28 days after transfusion.

Results. Participants were enrolled from June 3, 2020, through October 1, 2021. A total of 1225 participants underwent randomization, and 1181 received a transfusion. In the prespecified modified intention-to-treat analysis that included only participants who received a transfusion, the primary outcome occurred in 17 of 592 participants (2.9%) who received convalescent plasma and 37 of 589 participants (6.3%) who received control plasma (absolute risk reduction, 3.4 percentage points; 95% confidence interval, 1.0 to 5.8; P=0.005), which corresponded to a relative risk reduction of 54%. Evidence of efficacy in vaccinated participants cannot be inferred from these data because 53 of the 54 participants with Covid-19 who were hospitalized were unvaccinated and 1 participant was partially vaccinated. A total of 16 grade 3 or 4 adverse events (7 in the convalescent-plasma group and 9 in the control-plasma group) occurred in participants who were not hospitalized.

Conclusions. In participants with Covid-19, most of whom were unvaccinated, the administration of convalescent plasma within 9 days after the onset of symptoms reduced the risk of disease progression leading to hospitalization.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2119657?query=featured_coronavirus>

**title:** Short-term Outcomes of Corticosteroid Monotherapy in Multisystem Inflammatory Syndrome in Children

jama pediatrics | 28th march 2022

Question Is corticosteroid monotherapy a viable treatment alternative for multisystem inflammatory syndrome in children (MIS-C)?

Findings In this cohort study, patients receiving corticosteroids as initial management had similar rates of treatment failure compared with those receiving intravenous immunoglobulin plus corticosteroids, after adjusting for baseline presentation and disease severity; in the latter group, therapy failure due to laboratory parameters was more likely while failure due to cardiac parameters was less likely. Inpatient stay and corticosteroid course duration were shorter in patients initially treated with corticosteroid monotherapy.

Meaning In this study, corticosteroid monotherapy successfully treated a subset of patients with mild MIS-C.
<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2790362>

**infection control**

**title:** Risk of SARS-CoV-2 reinfections in children: a prospective national surveillance study between January, 2020, and July, 2021, in England

the lancet child & adolescent health|28th march 2022

Background. Reinfection after primary SARS-CoV-2 infection is uncommon in adults, but little is known about the risks, characteristics, severity, or outcomes of reinfection in children. We aimed to assess the risk of SARS-CoV-2 reinfection in children and compare this with the risk in adults, by analysis of national testing data for England.

Methods. In our prospective, national surveillance study to assess reinfection of SARS-CoV-2 in children in England, we used national SARS-CoV-2 testing data to estimate the risk of reinfection at least 90 days after primary infection from Jan 27, 2020, to July, 31, 2021, which encompassed the alpha (B.1.1.7) and delta (B.1.617.2) variant waves in England. Data from children up to age 16 years who met the criteria for reinfection were included. Disease severity was assessed by linking reinfection cases to national hospital admission data, intensive care admission, and death registration datasets.

Findings. Reinfection rates closely followed community infection rates, with a small peak during the alpha wave and a larger peak during the delta wave. In children aged 16 years and younger, 688 418 primary infections and 2343 reinfections were identified. The overall reinfection rate was 66·88 per 100 000 population, which was higher in adults (72·53 per 100 000) than children (21·53 per 100 000). The reinfection rate after primary infection was 0·68% overall, 0·73% in adults compared with 0·18% in children age younger than 5 years, 0·24% in those aged 5–11 years, and 0·49% in those aged 12–16 years. Of the 109 children admitted to hospital with reinfection, 78 (72%) had comorbidities. Hospital admission rates were similar for the first (64 [2·7%] of 2343) and second episode (57 [2·4%] of 2343) and intensive care admissions were rare (seven children for the first episode and four for reinfections). There were 44 deaths within 28 days after primary infection (0·01%) and none after reinfection.

Interpretation. The risk of SARS-CoV-2 reinfection is strongly related to exposure due to community infection rates, especially during the delta variant wave. Children had a lower risk of reinfection than did adults, but reinfections were not associated with more severe disease or fatal outcomes.
[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(22)00059-1/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642%2822%2900059-1/fulltext)

**title:** Importance of understanding the reinfection risk of COVID-19 in children

The Lancet Child & Adolescent Health| 28th march 2022

The Article by Anna A Mensah and colleagues addresses the important question of COVID-19 in children and the risk of reinfection over time in England. These data were collected before the emergence of the omicron variant of concern in England, but provide helpful insights into the overall picture of COVID-19, which has been quite different in children when compared with adults. Notably, with every decade of life there is an increasing risk of severe disease, including admission to hospital and death. This study also reinforces that the SARS-CoV-2 infection incidence in children is reflective of the trends observed in the community. The authors concluded that the risk of SARS-CoV-2 reinfection was strongly related to exposure due to community infection rates (particularly during the delta variant wave). They also noted that children had a lower risk of reinfection than did adults, but reinfections were not associated with more severe disease or fatal outcomes.

Children live with families or guardians and their school attendance and engagement in social networks are crucial to their development. The indirect effects of the pandemic on children, including the impact of COVID-19 on household family members, schooling, and mental health, are important to note. Hence, understanding the risk of reinfection in children is paramount, including the study finding that the reinfection rate was lowest in those not yet able to access a vaccine in most countries (ie, those younger than age 5 years). The lowest reinfection rate of 0·9 per 100 000 population was found in children younger than age 5 years, compared with 1·9 per 100 000 population in those aged 5–11 years and 5·5 per 100 000 population in those aged 12–16 years. These rates were 23, 11, and four times lower than in adults aged 20–29 years, who were unvaccinated and had the highest reinfection rate during that time period.

The methodology used in the study establishes a framework to review the effect of vaccines on reinfection by age groups, noting that countries such as Australia, Canada, and the USA have all commenced an mRNA vaccination programme in children aged 5–11 years, as have the UK as per advice from the Joint Committee on Vaccination and Immunisation (JCVI) on Feb 16, 2022. The JCVI recommendation is for children aged 5–11 years who have a clinical risk condition or are living wth someone who is immunosuporessed.

A limitation of this paper was that it did not capture the impact of reinfection on paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2, also known as multisystem inflammatory syndrome in children (MIS-C). This condition is a post inflammatory complication, occurring in children with a median age of 9 year and presenting about 2–6 weeks after SARS-CoV-2 infection. A single COVID-19 vaccine dose has reduced the number of MIS-C cases according to publications from France and the USA, and further study is required to investigate if this complication also occurs after reinfection. The study's finding that reinfection might not have been the reason for hospital admission (ie, patients might have been admitted to hospital with COVID-19, not because of COVID-19) is not unexpected. The medical history of paediatric readmission cases requires a detailed review of underlying co-morbidities and the final ICD-10 diagnoses. However, severe symptoms with COVID-19 are more common in those with a past medical history; in the study, the four children who had been admitted to an intensive care unit (ICU) following reinfection had also required intensive care during their primary infection. All four children had multiple and severe multisystem comorbidities and the authors could not ascertain the contribution of SARS-CoV-2 infection to the illness that eventually led to ICU admission. A publication by Ward and colleagues found that in the first year of the pandemic (2020), 51 children and adolescents in the UK were admitted to a paediatric ICU with COVID-19, and 91% of these children or adolescents had a pre-existing health condition. However, an important key finding of Mensah and colleagues' study is that reinfection with SARS-CoV-2 was not associated with fatal paediatric cases.

A potential area for future research is the role that rapid antigen testing might play in identifying cases of reinfection, especially as many countries have introduced routine screening (eg, in schools). Many of these reinfection cases will be asymptomatic, so their role in transmission at household, school, and community levels will be important to monitor, particularly if new variants of concern emerge. Finally, investigation of the role that multiple reinfections will have on the immune system in vaccinated individuals will be important, with a particular focus on the development of B cell and T cell immune memory.

The interplay between infection and vaccine will be crucial throughout 2022 and 2023 and will hopefully optimise protection across the life course and minimise the risk of reinfection (particularly that associated with severe disease), hospital admission, intensive care, and death.
[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(22)00093-1/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642%2822%2900093-1/fulltext)

**title:** How data from the United Kingdom has guided covid-19 vaccine policies

BMJ| 30th march 2022

Data from the NHS is playing a key role in guiding vaccination policies globally

Throughout the pandemic, the UK’s covid-19 data systems have been guiding global as well as local policies. The well established health information systems combined with the more recently established National Immunisation Management System in England provided timely information on infections, emergence of new variants, and the value of different interventions. But one of the most important contributions from the UK came from the ability to rapidly track vaccine effectiveness…
<https://www.bmj.com/content/376/bmj.o839>

**title:** Faith based dialogue can tackle vaccine hesitancy and build trust

BMJ| 21st FEBRUARY 2022

One in 10 Americans say that their religious beliefs prohibit them from getting covid-19 vaccines,1 and similar reports have emerged globally.2 Vaccine hesitancy tied to religious faith can undermine progress towards public safety,34 especially against a backdrop of increasing fervour for religious exemptions and ongoing misinformation about vaccine safety. As we continue to work on managing covid-19, however, the ability for multisectoral partnerships and faith based dialogue to have a positive role during the pandemic has been underestimated.

Diverse faith based forums can mitigate doubts about vaccines and promote constructive dialogue about health related decisions and public health safety. This kind of practical, community level dialogue is particularly needed to support the public’s decision making on vaccines. Learning from effective examples of collaboration can help healthcare providers listen to and communicate more effectively with religious communities during public health crises, especially when it comes to people from religious minorities who have historically been marginalised or silenced.

For many people, religion is a way of life and their leaders can be a trusted resource for health information—even more so, at times, than medical doctors or public health institutions. Although widespread variation exists, there are numerous religious communities and faith leaders who are compassionate allies with medicine and public health. In his August 2021 message, for example, Pope Francis urged Catholics to consider vaccination an “act of love,” calling it a “simple yet profound way to care for one another.”10 Other faith leaders have framed vaccinations as a moral imperative and an act towards a “common good” that benefits our interconnected global communities…
<https://www.bmj.com/content/376/bmj.o823>

**title:** Cellular responses to SARS-CoV-2 vaccination after B-cell depletion: conflicting results from studies

the lancet rheumatology| 1st april 2022

I read with interest the Article by Matthias Moor and colleagues evaluating humoral and cellular immune responses to SARS-CoV-2 mRNA vaccination in patients with a history of B-cell depletion. They described blunted humoral responses to vaccination in individuals with a variety of diseases treated with B-cell depletion, as reported now in numerous other studies. In addition, the authors reported blunted cellular responses in their study population and concluded that B-cell depletion impacts both the B-cell and T-cell response to SARS-CoV-2 vaccination. he report of blunted cellular responses to SARS-CoV-2 vaccination contrasts with other studies that have described either preserved or more robust cellular responses in patients on B-cell-depleting therapies than in healthy volunteers or those on other therapies.

The source of this discrepancy might relate to the methodology used—Moor and colleagues measured the amount of interferon γ (IFNγ) released following stimulation with SARS-CoV-2 peptides as opposed to measuring the number of cells producing IFNγ (via the enzyme-linked immune absorbent spot [ELISpot] assay as has been done in other studies. Alternatively, the Methods section of their Article states that they stimulated with peptide or mitogen for 1 h before the IFNγ ELISA measurement. This duration of stimulation is far shorter than the duration (16–24 h) recommended by the manufacturer (Qiagen, Hombrechtikon, Switzerland; category number 626715) and the time period in other assays. It is important to clarify whether this was an intentional departure from the suggested protocol or a typographical error.

Besides the methodology, other explanations for the discrepancies could be that, in the study by Moor and colleagues, some patients were taking additional immunosuppressive medication, such as steroids, calcineurin inhibitors, and antimetabolites, as well as B-cell-depleting therapies, which probably also affect the cellular response to vaccination. Indeed, studies on patients not receiving these additional agents show more robust cellular responses, suggesting that B-cell depletion alone

does not blunt this aspect of the immune response to SARS-CoV-2 vaccination. Perhaps the strongest evidence supporting this is the more robust cellular immune responses to SARS-CoV-2 vaccination in patients with X-linked agammaglobulinaemia than in healthy controls. Lastly, there are differences in demographic characteristics and treatments between the various conditions included in these studies, making it difficult to establish whether alterations in vaccine response might be driven primarily by the underlying disease.

Thus, it is important to understand whether the discrepant results pertaining to cellular responses to SARS-CoV-2 vaccination are related to methodological issues and to highlight that the observed blunted cellular responses could potentially be attributed to factors besides B-cell depletion.
[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00032-7/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913%2822%2900032-7/fulltext)

**title:** Factors associated with poor antibody response to third-dose SARS-CoV-2 vaccination in patients with rheumatic and musculoskeletal diseases

the lancet rheumatology | 21st FEBRUARY 2022

High coverage rates of vaccination against COVID-19 are envisaged to end the pandemic. However,
Many immunosuppressed patients with rheumatic and musculoskeletal disease have a poor antibody response to two-dose SARS-COV-2 mRNA vaccination, prompting widescale authorisation of a third vaccine dose for these patients. High antibody concentrations are required to overcome immune evasion by variants of concern in immunocompetent patients, and although a third dose augments the immune response against SARS-CoV-2 in some immunosuppressed patients it is uncertain whether this response is sufficient for protection. Thus, identifying patients with rheumatic and musculoskeletal disease with poor response following a third dose is important in the selection of appropriate candidates for further medical interventions such as additional vaccine doses or prophylactic therapies. Herein, we describe the antibody response and factors associated with poor antibody response following a third vaccine dose in immunosuppressed patients with rheumatic and musculoskeletal disease…
[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00065-0/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913%2822%2900065-0/fulltext)

**title:** Outcomes After SARS-CoV-2 Vaccination Among Children With a History of Multisystem Inflammatory Syndrome

jama network open| 28th march 2022

By reiterating the call from 2009 for raw clinical study data, Doshi and colleagues point out that,
Most children who contract SARS-CoV-2 are asymptomatic or mildly symptomatic.1 However, a subset of children subsequently develop a severe hyperinflammatory condition called multisystem inflammatory syndrome in children (MIS-C) 4 to 6 weeks after having COVID-19.2 The underlying mechanisms of MIS-C remain unclear,3 leading to hesitation to vaccinate children with a history of MIS-C against SARS-CoV-2 because of concerns for a reoccurrence of hyperinflammation. In December 2020, the US Food and Drug Administration and the Italian Drug Agency (Agenzia Italiana del Farmaco) provided emergency use authorization for the COVID-19 vaccine, BNT162b2, in individuals 16 years or older. In May 2021, the vaccine became available to individuals 12 years or older. We aimed to evaluate outcomes following SARS-CoV-2 vaccination in patients previously diagnosed with MIS-C and hypothesized that vaccination would be well-tolerated…

…In this study, 15 patients treated for MIS-C after COVID-19 tolerated vaccination against SARS-CoV-2 without developing hyperinflammation, myocarditis, or reoccurrence of MIS-C up to 9.5 months after vaccination. This study provides critical information while the COVID-19 pandemic continues now that SARS-CoV-2 vaccination is available to children in the age range most at risk of developing MIS-C.2 Because of the rarity of MIS-C, our study is limited by a small sample size and its retrospective nature. However, with the known additive protection from reinfection provided by vaccinating previously infected individuals,6 these findings suggest that patients with a history of MIS-C can be offered vaccination against SARS-CoV-2.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790426>

**title:** Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection

new england journal of medicine | 31st march 2022

Background. The duration and effectiveness of immunity from infection with and vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are relevant to pandemic policy interventions, including the timing of vaccine boosters.

Methods. We investigated the duration and effectiveness of immunity in a prospective cohort of asymptomatic health care workers in the United Kingdom who underwent routine polymerase-chain-reaction (PCR) testing. Vaccine effectiveness (≤10 months after the first dose of vaccine) and infection-acquired immunity were assessed by comparing the time to PCR-confirmed infection in vaccinated persons with that in unvaccinated persons, stratified according to previous infection status. We used a Cox regression model with adjustment for previous SARS-CoV-2 infection status, vaccine type and dosing interval, demographic characteristics, and workplace exposure to SARS-CoV-2.

Results. Of 35,768 participants, 27% (9488) had a previous SARS-CoV-2 infection. Vaccine coverage was high: 95% of the participants had received two doses (78% had received BNT162b2 vaccine [Pfizer–BioNTech] with a long interval between doses, 9% BNT162b2 vaccine with a short interval between doses, and 8% ChAdOx1 nCoV-19 vaccine [AstraZeneca]). Between December 7, 2020, and September 21, 2021, a total of 2747 primary infections and 210 reinfections were observed. Among previously uninfected participants who received long-interval BNT162b2 vaccine, adjusted vaccine effectiveness decreased from 85% (95% confidence interval [CI], 72 to 92) 14 to 73 days after the second dose to 51% (95% CI, 22 to 69) at a median of 201 days (interquartile range, 197 to 205) after the second dose; this effectiveness did not differ significantly between the long-interval and short-interval BNT162b2 vaccine recipients. At 14 to 73 days after the second dose, adjusted vaccine effectiveness among ChAdOx1 nCoV-19 vaccine recipients was 58% (95% CI, 23 to 77) — considerably lower than that among BNT162b2 vaccine recipients. Infection-acquired immunity waned after 1 year in unvaccinated participants but remained consistently higher than 90% in those who were subsequently vaccinated, even in persons infected more than 18 months previously.

Conclusions. Two doses of BNT162b2 vaccine were associated with high short-term protection against SARS-CoV-2 infection; this protection waned considerably after 6 months. Infection-acquired immunity boosted with vaccination remained high more than 1 year after infection.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2118691>

**title:** Effectiveness of the BNT162b2 Vaccine after Recovery from Covid-19

new england journal of medicine | 31st march 2022

Background. The risk of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) decreases substantially among patients who have recovered from coronavirus disease 2019 (Covid-19). However, it is unknown how long protective immunity lasts. Current guidelines recommend vaccination of recovered patients even though data regarding vaccine effectiveness in such cases are still limited.

Methods. In this retrospective cohort study, we reviewed electronic medical records from a large health care organization in Israel to assess reinfection rates in patients who had recovered from SARS-CoV-2 infection before any vaccination against Covid-19. We compared reinfection rates among patients who had subsequently received the BNT162b2 vaccine (Pfizer–BioNTech) and those who had not been vaccinated between March 1 and November 26, 2021. We used a Cox proportional-hazards regression model with time-dependent covariates to estimate the association between vaccination and reinfection after adjustment for demographic factors and coexisting illnesses. Vaccine effectiveness was estimated as 1 minus the hazard ratio. In a secondary analysis, we evaluated the vaccine effectiveness of one dose as compared with two doses.

Results. A total of 149,032 patients who had recovered from SARS-CoV-2 infection met the eligibility criteria. Of these patients, 83,356 (56%) received subsequent vaccination during the 270-day study period. Reinfection occurred in 354 of the vaccinated patients (2.46 cases per 100,000 persons per day) and in 2168 of 65,676 unvaccinated patients (10.21 cases per 100,000 persons per day). Vaccine effectiveness was estimated at 82% (95% confidence interval [CI], 80 to 84) among patients who were 16 to 64 years of age and 60% (95% CI, 36 to 76) among those 65 years of age or older. No significant difference in vaccine effectiveness was found for one dose as compared with two doses.

Conclusions. Among patients who had recovered from Covid-19, the receipt of at least one dose of the BNT162b2 vaccine was associated with a significantly lower risk of recurrent infection.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2119497>

**title:** BNT162b2 Protection against the Omicron Variant in Children and Adolescents

new england journal of medicne | 30th march 2022

Background. Spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B.1.1.529 (omicron) variant, which led to increased U.S. hospitalizations for coronavirus disease 2019 (Covid-19), generated concern about immune evasion and the duration of protection from vaccines in children and adolescents.

Methods. Using a case–control, test-negative design, we assessed vaccine effectiveness against laboratory-confirmed Covid-19 leading to hospitalization and against critical Covid-19 (i.e., leading to receipt of life support or to death). From July 1, 2021, to February 17, 2022, we enrolled case patients with Covid-19 and controls without Covid-19 at 31 hospitals in 23 states. We estimated vaccine effectiveness by comparing the odds of antecedent full vaccination (two doses of BNT162b2 messenger RNA vaccine) at least 14 days before illness among case patients and controls, according to time since vaccination for patients 12 to 18 years of age and in periods coinciding with circulation of B.1.617.2 (delta) (July 1, 2021, to December 18, 2021) and omicron (December 19, 2021, to February 17, 2022) among patients 5 to 11 and 12 to 18 years of age.

Results. We enrolled 1185 case patients (1043 [88%] of whom were unvaccinated, 291 [25%] of whom received life support, and 14 of whom died) and 1627 controls. During the delta-predominant period, vaccine effectiveness against hospitalization for Covid-19 among adolescents 12 to 18 years of age was 93% (95% confidence interval [CI], 89 to 95) 2 to 22 weeks after vaccination and was 92% (95% CI, 80 to 97) at 23 to 44 weeks. Among adolescents 12 to 18 years of age (median interval since vaccination, 162 days) during the omicron-predominant period, vaccine effectiveness was 40% (95% CI, 9 to 60) against hospitalization for Covid-19, 79% (95% CI, 51 to 91) against critical Covid-19, and 20% (95% CI, −25 to 49) against noncritical Covid-19. During the omicron period, vaccine effectiveness against hospitalization among children 5 to 11 years of age was 68% (95% CI, 42 to 82; median interval since vaccination, 34 days).

Conclusions. BNT162b2 vaccination reduced the risk of omicron-associated hospitalization by two thirds among children 5 to 11 years of age. Although two doses provided lower protection against omicron-associated hospitalization than against delta-associated hospitalization among adolescents 12 to 18 years of age, vaccination prevented critical illness caused by either variant.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2202826?query=featured_coronavirus>

**title:** Effectiveness of SARS-CoV-2 vaccines in the post-natural infection world

the lancet infectious diseases | 31st march 2022

Natural viral infections provide immunity from subsequent infection through a repertoire of memory T cells and B cells, except when the virus mutates to an extent that it evades recognition by memory cells. Vaccines are designed to represent the virus either in the form of an inactivated or attenuated whole virus or an immunogenic subunit such as the spike protein in the case of SARS-CoV-2. After a natural infection, the immune system assesses the virus in multiple ways and provides both antibody-mediated and cellular protection.

As the SARS-CoV-2 pandemic has relentlessly progressed, with multiple waves, the immune landscape of the global population has transformed from being immune naive to having natural infection-induced immunity. Although vaccinating the naive population is logical, an important question arises of whether to vaccinate those who were previously infected with SARS-CoV-2. The need for boosting natural immunity, through vaccination, comes from the waning of immunity, with declining antibody titres, and the emergence of SARS-CoV-2 variants with immune-evasion properties.

In The Lancet Infectious Diseases, Thiago Cerqueira-Silva and colleagues have addressed the issue of vaccine effectiveness among individuals who were previously infected. For this study, the authors used national COVID-19 notification, hospitalisation, and vaccination datasets from Brazil to assess effectiveness against symptomatic infection, hospitalisation, and death for the four vaccines in use in the country during the study period: CoronaVac (Sinovac), ChAdOx1 nCoV-19 (Oxford-AstraZeneca), Ad26.COV2.S (Janssen), and BNT162b2 (Pfizer-BioNtech). Of the people who had previous confirmed SARS-CoV-2 infection, the authors included 22 566 symptomatic individuals with RT-PCR-positive reinfection and 145 055 negative RT-PCR tests from 68 426 symptomatic matched controls in a test-negative case-control study. After adjusting for important confounders, vaccine effectiveness against symptomatic infection 14 days or more from complete vaccination after a previous natural infection was 39·4% (95% CI 36·1–42·6) for CoronaVac, 56·0% (51·4–60·2) for ChAdOx1 nCoV-19, 44·0% (31·5–54·2) for Ad26.COV2.S (single-dose vaccine), and 64·8% (54·9–72·4) for BNT162b2. Vaccine effectiveness against hospitalisation or death after complete vaccination was more impressive: 81·3% (75·3–85·8) for CoronaVac, 89·9% (83·5–93·8) for ChAdOx1 nCoV-19, 57·7% (−2·6 to 82·5) for Ad26.COV2.S, and 89·7% (54·3–97·7) for BNT162b2.

The study has some major strengths. First, the linkage of three national databases for SARS-CoV-2 testing, disease surveillance for COVID-19, and immunisation. This showcases the importance of population-level data and the power of big-data analysis. Second, the comprehensive evaluation of vaccine effectiveness of four vaccines used globally. And third, the study of the dose–response relationship. However, an important missing piece of information is the SARS-CoV-2 variants against which vaccine effectiveness estimates are reported. This absence is important in view of variable vaccine effectiveness against different variants.

The vaccine effectiveness estimates in the study by Cerqueira-Silva and colleagues are generally lower than those in naive populations reported earlier.

However, this discrepancy is expected given that Cerqueira-Silva and colleagues' estimates were for additional protection provided by vaccination over and above that offered by immunity resulting from natural infection. Natural infection might act as a priming or booster dose; in a previous study, protection against reinfection was maintained at greater than 90% for more than 6 months after vaccination among participants with natural immunity who were subsequently vaccinated, even in those who were infected more than 12 months before vaccination. Protection as high as 82%, similar to two vaccine doses, was shown in individuals previously infected who had received a single dose of vaccine. These clinical findings are corroborated by in-vitro immunological studies showing that humoral and cellular immune responses are high after the multiple antigen exposure provided by natural infection and vaccination.10 In addition to antibody-mediated immunity, cellular T-cell responses provide protection against severe disease, hospitalisation, and death. The results of Cerqueira-Silva and colleagues' study and other recent studies challenge the concept of population-level herd immunity through natural infection alone against SARS-CoV-2 and suggest that vaccinating individuals who were previously infected provides further protection, particularly against severe disease. These data should help guide policy decisions and mitigate vaccine hesitancy among people who have previously had SARS-CoV-2 infection.

However, some clinical and immunological questions remain to be answered. Primary exposure to an antigen leads to epitope-specific B-cell memory known as immune imprinting. Barring the ancestral virus infection, subsequent SARS-CoV-2 infections during multiple waves caused by variants have led to heterologous exposure to virus antigens. How immune imprinting by the first exposure, either by the virus or vaccine, affects the durability and breadth of immune responses remains to be studied. What additional protection does natural infection provide to vaccinated individuals and how durable is this protection? And what is the optimal timing of vaccination after natural infection? These questions are important in view of the large swath of the global population who have been exposed to natural infections caused by delta (B.1.617.2) and omicron (B.1.1.529) variants.

Hybrid immunity due to exposure to natural infection and vaccination is likely to be the norm globally and might provide long-term protection even against emerging variants. Besides vaccination, continued surveillance for further emergence of variants for their immune evasiveness and pathogenicity should continue.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00207-9/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900207-9/fulltext)

**title:** Interplay of infection and vaccination in long-term protection from COVID-19

the lancet infectious diseases | 31st march 2022

The SARS-CoV-2 omicron variant has rapidly spread throughout the world, including in countries with high vaccination rates. As populations increasingly include individuals with both vaccination-driven and infection-driven immunity, it becomes important to understand the differential protection associated with diverse immune histories. Although studies assessing long-term immunity after omicron infection are not yet possible, population-wide studies done in the context of previous variants of concern can be highly informative. In The Lancet Infectious Diseases, Peter Nordström and colleagues use Swedish national infection and vaccination registers to assess population-wide protection from SARS-CoV-2 infection up to October, 2021. Using a cohort of more than 2 million individuals, they showed that infection-associated immunity was 95% protective against subsequent reinfection during 20 months of follow-up compared with no immunity (adjusted hazard ratio [aHR] 0·05 [95% CI 0·05–0·05] p<0·001). In comparison, convalescent individuals who received one dose of a COVID-19 vaccine exhibited a further 58% lower risk of reinfection (aHR 0·42 [95% CI 0·38–0·47]; p<0·001), albeit it with some degree of waning over the next 9 months of follow-up. Convalescent individuals receiving two doses of a vaccine benefitted from only marginally greater protection (aHR 0·34 [95% CI 0·31–0·39]; p<0·001) than those who received one dose (aHR 0·42 [95% CI 0·38–0·47]; p<0·001), with a 66% lower risk of reinfection than those in the infection-only cohort.

These data show, in a large cohort, the added protective benefit of vaccination among individuals recovered from COVID-19. Although the difference in protection between the one-dose and two-dose vaccine groups was reasonably small, Nordstrom and colleagues found some evidence for greater waning of protection among the single-dose group than the two-dose group. In both cases, there was at least 90% reduction in the risk of COVID-19-associated hospitalisation compared with the convalescent cohort. A substantial benefit related to the large sample size of this population-wide study is the ability to also assess the risk of reinfection among specified subgroups. In particular, protection from previous infection was weaker in individuals aged 65 years and older, suggesting that vaccination might be particularly important in some high-risk populations; this is probably particularly true for protection against omicron, in which a third vaccine dose is key to eliciting cross-reactive neutralising antibodies. On balance, these data clearly show the benefits of two-dose vaccination for convalescent individuals, both in terms of the durability of immunity and protection from severe disease.

The data also show the long-term protective effect of SARS-CoV-2 infection alone, which was stable for 20 months of follow-up. This level of protection was notable, considering the wide range of neutralising antibody titres generated by mild COVID-19. The authors note that, given these results, infection history should be accounted for when so-called immunity passports are required for individuals to partake in wider societal activities. Although these analyses cannot take into account the effect of vaccination on viral transmission to others, immune profiles should, at the very least, be informative in assessing an individual's risk of subsequent reinfection, regardless of the nature of previous antigen exposure.

As the pandemic continues to evolve, the nature of population-wide immunity against SARS-CoV-2 will become increasingly complex. Due to the immune evasion of the omicron variant driving an increasing number of breakthrough infections, combined with varying recommendations for third or fourth vaccine doses, many populations will exhibit a mixture of infection-elicited and vaccine-elicited immunity. Although Nordstrom and colleagues focus on the protection associated with infection followed by vaccination, many individuals will now have vaccination followed by infection. A recent study however, showed that regardless of whether infection occurs before or after vaccination, the quantity, quality, and breadth of the humoral immune response were vastly improved. This finding further supports the notion that infection histories should be an important consideration in determining whether individuals are protected against SARS-CoV-2. Future studies will be required to assess whether infection by distinct viral variants imparts differing levels of protective immunity, and to better understand the epidemiological effect of infection across different variant waves.

Looking forward, the incorporation of infection history in an immune profile of an individual, although justified, brings into question how future booster regimens should be planned for. For instance, are individuals with infection-associated immunity required to obtain two further doses to have the level of immunity observed in individuals with no previous infection but receiving three doses? Regardless, SARS-CoV-2 infection is clearly an important contributor to protective immunity, and its interplay with vaccination warrants further longitudinal studies, ultimately providing insights to drive proactive health policies and measures for optimal population-wide immunity in this pandemic.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00210-9/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900210-9/fulltext)

**title:** DNA vaccines join the fight against COVID-19

the lancet| 2nd april 2022

…Despite decades of research and development of DNA vaccines, including at least eight candidates currently in clinical trials for COVID-19 they have had limited success. One of the main challenges for DNA vaccines is the delivery: mRNA vaccines need to cross only one membrane to reach their site of action (cytoplasm), whereas DNA vaccines need to cross the cytoplasm and the nuclear membrane. Because of this difference, the lipid nanoparticles that effectively deliver mRNA do not work as well for DNA. Historically, DNA vaccines have required a physical method of delivery such as electroporation, or the needle-free injection system used in this study. Although these physical devices appear to be effective—as shown in this study—they pose a potential challenge for widespread use and scale-up. The device used in Khobragade and colleagues’ study is small and portable (<50 g) and consists of an injector, syringe, and filling adapter. However, widespread administration of ZyCoV-D will be limited not only by production and availability of the DNA, but also the injection device, which is vulnerable to global manufacturing disruptions. If these delivery system challenges can be overcome then the amenable storage conditions, efficacy against COVID-19 (including the delta strain), and low cost (<US$10) have poised ZyCoV-D to be another global solution in our fight against SARS-CoV-2, and might act as a catalyst for DNA-based vaccines against other diseases, such as tuberculosis and HIV-1, especially in areas that have restricted access and affordability.
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00524-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2900524-4/fulltext)

**title:** Efficacy, safety, and immunogenicity of the DNA SARS-CoV-2 vaccine (ZyCoV-D): the interim efficacy results of a phase 3, randomised, double-blind, placebo-controlled study in India

the lancet | 2nd april 2022

Background. ZyCoV-D, a DNA-based vaccine, showed promising safety and immunogenicity in a phase 1/2 trial. We now report the interim efficacy results of phase 3 clinical trial with ZyCoV-D vaccine in India.

Methods. We conducted an interim analysis of a multicentre, double-blind, randomised, placebo-controlled phase 3 trial at 49 centres in India. Healthy participants aged at least 12 years were enrolled and randomly assigned (1:1) to receive either ZyCov-D vaccine (Cadila Healthcare; 2 mg per dose) or placebo. An interactive web response system was used for randomisation (blocks of four) of participants as well as to enrol those aged 60 years and older with or without comorbid conditions, and those aged 12–17 years. It was also used to identify 600 participants for immunogenicity (blocks of six). Participants, investigators, and outcome assessors were masked to treatment assignment. Three doses of vaccine or placebo were administered intradermally via a needle-free injection system 28 days apart. The primary outcome was the number of participants with first occurrence of symptomatic RT-PCR-positive COVID-19 28 days after the third dose, until the targeted number of cases (interim analysis n=79, full analysis n=158) have been achieved. The analysis was done in the per-protocol population, which consisted of all participants with negative baseline SARS-CoV-2 status who received three doses of vaccine or placebo. Assessment of safety and tolerability was based on the safety population, which consisted of all enrolled participants who were known to have received at least one dose of study vaccine or placebo. This trial is registered with Clinical Trial Registry India, CTRI/2021/01/030416, and is ongoing.

Findings. Between Jan 16, and June 23, 2021 (data cutoff), 33 194 individuals were screened, of whom 5241 did not meet screening criteria and 27 703 were enrolled and randomly assigned to receive ZyCoV-D (n=13 851) or placebo (n=13 852). Per-protocol, 81 cases were eligible and included in efficacy analysis (20 of 12 350 in the ZyCoV-D group and 61 of 12 320 in placebo group). The ZyCoV-D vaccine efficacy was found to be 66·6% (95% CI 47·6–80·7). The occurrence of solicited adverse events was similar between the treatment groups (623 [4·49%] in the ZyCoV-D group vs 620 [4·47%] in the placebo group). There were two deaths (one in each group) reported at the data cutoff, neither of which was considered related to the study treatments.
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00151-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2900151-9/fulltext)

**title:** Serum neutralisation of the SARS-CoV-2 omicron sublineage BA.2

the lancet microbe | 28th march 2022

The government has just announced that all covid-19 restrictions in England are set to end. Boris
The rapidly emerging SARS-CoV-2 omicron variant is associated with high transmissibility, compromised serum neutralising activity, and reduced vaccine effectiveness. BA.1 is the dominant omicron sublineage, making up more than 97% of omicron variant sequences worldwide in November and December, 2021, whereas BA.2 and BA.3 were rare. Hence, early studies of the omicron variant were mainly based on the BA.1 sublineage. Since early January, 2022, there has been a sudden upsurge of BA.2 in Europe and Asia, accounting for 15·6% of omicron variant sequences detected at the end of January, 2022. In view of the increasing epidemiological importance, there is an urgent need to assess the serum neutralising activity against BA.2, which correlates with vaccine effectiveness…

…Our data indicate that the immune escape from BA.2 is not as severe as from BA.1, suggesting that other viral or host factors are driving the rapid spread of BA.2. Since NAb titres correlate with vaccine effectiveness, our data suggest that currently available vaccines might be more effective against BA.2 than BA.1. This study was approved by the institutional review board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW 13–265 and UW 21–214) and the Hospital Authority Kowloon West Cluster (KW/EX-20–038[144–26]). Written informed consent was obtained from all study participants.
[https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(22)00060-X/fulltext](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247%2822%2900060-X/fulltext)

**HEALTH MANGEMENT & SERVICES**

**title:** Covid-19: Oxygen shortages two years into pandemic highlight pre-covid failures, says WHO

BMJ| 29th march 2022

While the UK’s perceived pandemic missteps abound, the country was truly “world beating” in at
Two years into the covid-19 pandemic, access to oxygen is still a major problem in low and middle income countries, health leaders have warned.

The shortages have highlighted the “abject failure” of the global community to develop and build up primary healthcare and universal health coverage over the past 20 years, said Michael Ryan, the World Health Organization’s health emergencies programme executive director.

“Covid didn’t cause this, covid uncovered this. Covid laid bare, tore away the bandages from, some very, very old wounds,” Ryan told an Access to Covid-19 Tools (ACT) Accelerator briefing. “No one was interested in oxygen,” he said, despite it being vital for the treatment of patients with covid-19 in the early stages of the pandemic.
<https://www.bmj.com/content/376/bmj.o829>

**recovery**

**title:** An open letter to the Executive Board of WHO from the surgical and anaesthesia community

the lancet | 28th march 2022

This Viewpoint explains how some hospitals used home monitoring of pulse oximetry during the
An estimated 28 million surgeries were cancelled worldwide during the first 3 months of the COVID-19 pandemic, a number which might now be as high as 115 million—more than a third of all surgeries annually. We applaud the work of WHO over the past 2 years in managing and reducing the impacts of the pandemic, but are critical about the efforts taken to mitigate the impact of cancelled surgeries despite the recognition of surgery as an essential part of universal health coverage. Given the unequal impacts the pandemic has had across clinical disciplines, countries, and populations, we strongly support the development of a binding worldwide pandemic treaty.

With the sharp rise in non-communicable diseases worldwide, the demand for surgical care is rapidly increasing. Surgical interventions are needed for 80% of injured patients and more than half of patients with cancer.

Given the high versatility and the clear value surgical teams and infrastructure have added to the pandemic response, it is surprising that surgical system strengthening has not received more attention as part of pandemic preparedness initiatives thus far. We suggest a paradigm shift where access to surgical care is mainstreamed into pandemic preparedness policies. A mainstreaming approach would entail that the pandemic treaty assures that every policy adopted or implemented from this treaty has been evaluated for its impact on national-level surgical care provision. Only policies that do not harm surgical care provision should be included in the final version of the treaty so as to avoid detrimental impact. While novel in global surgery discourse, this would entail a policy approach similar to WHO's Health in All Policies…
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00521-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2900521-9/fulltext)

**title:** Covid-19: Taxpayers are still liable for £2.7bn risk from government PPE contracts, say auditors

bmj | 30th march 2022

The NHS has been warned. the additional funding announced by the government comes with billions of pounds of taxpayers’ money are still at risk from contracts for personal protective equipment (ppe) that were hurriedly signed in 2020 to respond to the covid pandemic, the government’s public spending watchdog has concluded. In a report published on 31 March the National Audit Office (NAO) said that financial fallout was still being felt from the “extremely overheated” global market in 2020 that had pushed up PPE prices.

Gareth Davies, head of the NAO, said, “The Department of Health and Social Care is still dealing with the results of its emergency procurement decisions, some two years after it first needed to rapidly buy ppe in unprecedented circumstances. The department is continuing to manage 176 contracts where it believes it may not achieve full value for money, with an estimated £2.7bn [€3.2bn; $3.6bn] at risk.”..
<https://www.bmj.com/content/376/bmj.o837>

**title:** Investigation Into The Management Of PPE Contracts

national audit office | 30th march 2022

According to this report, the Department of Health & Social Care (DHSC) continues to deal with the contract management issues caused by the need to purchase unprecedented volumes of PPE in 2020 due to Covid-19, with billions of pounds of taxpayers’ money still at risk. It finds that since February 2020 DHSC and its NHS procurement partner, NHS Supply Chain Co-ordination Limited, have awarded almost 10,000 contracts for personal protective equipment (PPE). DHSC has so far spent £12.6 billion of the total £13.1 billion it expects to spend on almost 38 billion items of PPE. It also outlines how DHSC is continuing to assess potential fraud across the programmes and its current estimate is that this will be between 0.5 per cent and 5.0 per cent of expenditure. <https://kingsfund.blogs.com/health_management/2022/03/investigation-into-the-management-of-ppe-contracts.html>

**title:** Should covid-19 vaccines and drugs be “not for profit”?

bmj | 30th march 2022

HIV, Ebola, and now covid-19: if a pandemic is not the time for governments to retain control by sharing knowledge and waiving intellectual property rules, then when, asks Mohga Kamal-Yanni. But Thomas Cueni says that debates about prices and profit are straw men to the real question of why the world failed to provide equitable access to covid vaccines…
<https://www.bmj.com/content/376/bmj.o755>

**title:** Mixed response to COVID-19 intellectual property waiver

the lancet | 2nd april 2022

A tentative compromise deal brokered in trade talks between the EU, the USA, India, and South Africa (the Quad) on a World Trade Organization (WTO) intellectual property waiver for COVID-19 vaccines has drawn mixed responses. The agreement authorises eligible WTO members to use patented ingredients and processes for the production and supply of COVID-19 vaccines without the consent of the right holder. The draft text says that WTO members will decide on its extension to cover COVID-19 diagnostics and therapeutics no later than 6 months from the date of the decision on vaccines. The duration of the waiver is also still not agreed on and could be for a 3-year or 5-year period.
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00610-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2900610-9/fulltext)

**title:** Reducing “COVID-19 Misinformation” While Preserving Free Speech

jama | 31st march 2022

Misinformation about risks, prevention, and treatment of COVID-19 has cost lives. Misinformation comes from many sources, with many motives for spreading and believing it. In caring capably and compassionately for patients, a substantial majority of health professionals and health care organizations have vigorously defended the standards of medical science and public health practice. However, a vocal minority and their sponsors or allies have exploited their medical credentials to the detriment of the public. They have understated known risks of severe illness, challenged the safety and effectiveness of vaccines without evidence, touted unproved and risky treatments, and amplified conspiracy theories about science and scientists. These activities have compounded the ethical stress and moral injury the health care workforce has experienced during repeated pandemic surges.
<https://jamanetwork.com/journals/jama/fullarticle/2790859>

**workforce wellbeing**

**title:** Covid-19: NHS staff will still have access to free tests

bmj | 30th march 2022

The UK government has announced an end to all covid-19 restrictions in England, saying that
NHS and care staff, as well as some vulnerable patients, will continue to have access to free testing for covid-19 in a move that has been welcomed as a victory for common sense.

In February it was announced that free covid testing would end for most people in England from 1 April under the government’s Living with Covid plan.1 The BMA and the NHS Confederation have been calling for NHS staff to continue to have access to free testing, and they welcomed the latest decision even though it came at the “11th hour.” England’s health secretary, Sajid Javid, has announced that free symptomatic testing will be provided for people living or working in some high risk settings, including staff in the NHS, in care homes and hospices, and in prisons and places of detention.2 People will also be tested before being discharged from hospital into care homes, hospices, homelessness settings, or domestic abuse refuges.

Free symptomatic testing will also be provided for patients in hospital, where a PCR test is required for patient care, and to provide access to treatments and support ongoing clinical surveillance for new variants. Patients with a higher risk of getting seriously ill from covid will also be contacted directly and sent lateral flow tests to keep at home for use if they have symptoms.

Under the plans asymptomatic lateral flow testing will continue from April in “some high risk settings where infection can spread rapidly while prevalence is high.” This includes patient facing NHS staff, as well as NHS commissioned independent healthcare providers, staff in hospices and adult social care services, a small number of care home visitors who provide personal care, some prison staff, and staff in high risk domestic abuse refuges and homelessness settings. Testing will also be provided for care home staff and residents during an outbreak and for care home residents on admission.

The government said that it had retained the ability to enable a rapid testing response if needed, such as for a new variant of concern. This includes maintaining a stockpile of lateral flow tests and the ability to ramp up testing laboratories and delivery channels.

It added that the Community Infection Survey, delivered by the Office for National Statistics, would continue to monitor infection levels, as would the Vivaldi study in residential care homes, the Siren study in the NHS, and surveillance in primary care by the Royal College of General Practitioners. The government’s Therapeutics Taskforce and Antiviral Taskforce will be merged into a single unit.

Roles not segregated. Covid-19 infections and hospital admissions have been rising in recent weeks. However, the government said that over 55% of people in hospital who had tested positive were not there with covid-19 as their primary diagnosis.

Jenny Harries, chief executive of the UK Health Secretary Agency, said, “As we learn to live with covid, we are focusing our testing provision on those at higher risk of serious outcomes from the virus, while encouraging people to keep following simple steps to help keep themselves and others safe.”

Under the new guidance from 1 April anyone with symptoms of a respiratory infection including covid-19, who also has a high temperature or feels unwell, should stay at home and avoid contact with other people until they feel well enough to resume normal activities and no longer have a high temperature.

The BMA said it was a relief that ministers had abandoned plans to scrap testing for healthcare workers altogether but that restricting testing to those in patient facing roles ignored the reality of working life.

Chaand Nagpaul, BMA chair of council, said, “Staff in patient facing roles or otherwise are not segregated and therefore can easily spread infection between each other. By artificially making this distinction we also risk pushing up staff absence rates, which are already impacting on services and patient care.

“We are also concerned that the guidance states free testing can occur when there is a ‘high prevalence’ of infection—but there is no clarity in the statement on the definition of a ‘high prevalence.’ This needs to be made clear as soon as possible, given the current high infection rates across society.”

Two tier society. The BMA is also concerned that elderly people are not included in the group given access to free testing, nor those who come into contact with vulnerable people. It also warned that there was no provision for free testing based on affordability and that this risked creating a two tier society based on who could afford to pay for tests. Welcoming the decision, Matthew Taylor, chief executive of the NHS Confederation, said, “Health leaders will be relieved that the government has seen sense and confirmed at the 11th hour that NHS staff in patient facing roles will continue to have access to free testing against covid-19. This is a victory for common sense.”

Saffron Cordery, deputy chief executive of NHS Providers, also welcomed the decision but said that it had come late in the day. “Rising covid cases are putting increased pressure on NHS services, which also face high staff absence rates,” she said. “This is having a knock-on impact on how fast trusts can deliver backlog recovery.”

Cordery added that the end of universal free testing could affect the ambition to reduce health inequalities. “There is a risk that we may see a two tier system where those who cannot afford to pay for tests are at greater risk of catching the virus. No one should have to make a choice between their health or heating,” she said.
<https://www.bmj.com/content/376/bmj.o851>

**title:** Scrapping free covid tests for NHS staff is completely wrong

BMJ| 29th MArch 2022

The covid-19 pandemic has pushed the NHS and its staff to their limit

Healthcare workers battled to keep patients safe as hospitals overflowed. GPs, hospital doctors, and community staff regularly wore their own makeshift protection when personal protective equipment (PPE) supplies weren’t good enough, and many sacrificed their own wellbeing as they worked every hour they could to look after their patients and keep the health service afloat. Tragically, some even gave their lives.

Now, just two years after what has been a traumatic experience for all healthcare staff, they don’t know if they will be able to carry on accessing free lateral flow tests from 1 April 2022.

In February, NHS England said they would “communicate further about testing provision for NHS staff and patients,” but there have so far been no assurances that staff will still be able to access free tests—or who is going to pay for it.1 We’re just four days away now and desperately need this guidance. The BMA is urgently calling for free testing for healthcare staff to continue.

Under current rules, NHS staff are required to test themselves for covid twice a week and report the results before coming into work; an invaluable tool for monitoring prevalence of the disease and most importantly, protecting patients if a staff member has covid. These tests are currently provided for free when ordered online or from community pharmacies.

Without this, covid would be allowed to spread unchecked—and it’s already on the rise. The Office for National Statistics (ONS) estimates that more than three million people currently have the virus in England. The number of people in hospital is also increasing, with 17 685 currently receiving care.

Free testing is a key tool for measuring prevalence of covid-19 among the public, as well as limiting the spread of infection, and we believe this should continue. It is particularly important to make lateral flow tests freely available for those who come into contact with people who are at highest risk from covid-19, including the clinically vulnerable, to protect them from infection…
<https://www.bmj.com/content/376/bmj.o830>

**title:** Pushed to Their Limits, 1 in 5 Physicians Intends to Leave Practice [US]

jama | 30th march 2022

On the same day in March 2020 that President Donald Trump declared the COVID-19 pandemic a national emergency, researchers at the Larry A. Green Center in Virginia launched an ongoing survey of COVID-19’s effects on primary care practices. Over the past 2 years, more than 36 000 survey responses from clinicians across the country have painted an alarming picture of a workforce that’s increasingly burned out, traumatized, anxious, and depressed. As Green Center codirector Rebecca S. Etz, PhD, summed up her survey’s findings in a recent interview with JAMA, “It’s been bad for primary care over the pandemic and it’s getting worse.”…
<https://jamanetwork.com/journals/jama/fullarticle/2790791>

**public health**

**title:** COVID-19 Infection Among Incarcerated Individuals and Prison Staff in Lombardy, Italy, March 2020 to February 2021

jama network open | 30th march 2022

Question What was the COVID-19 infection rate among incarcerated individuals and staff during the first pandemic year in the prison system in Lombardy, Italy, when infection prevention measures had been implemented?

Findings In this cross-sectional study including a mean population of 7599 incarcerated individuals and 4591 staff members of 18 prisons in Lombardy, case rate and relative risk were significantly higher in incarcerated individuals and prison staff than the general population. Significant correlations between assessed control measures and case rate in incarcerated individuals were not found.

Meaning The findings of this study suggest that prison settings need to be included and prioritized in the framework of emergency preparedness and response.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790504>

**HEALTH INEQUALITIES**

**title:** The world’s refugees remain last in line for covid-19 vaccines

bmj | 29th march 2022

Neither supply nor hesitancy is a major barrier to covid-19 vaccination for the world’s displaced people, report Sally Howard and Geetanjali Krishna…

…Two years into the pandemic, 34.7% of the world’s population have not had a single dose of vaccine.1 For vulnerable groups such as refugees and internally displaced persons—85% of whom are hosted in low and middle income countries—the disparity in comparison with the citizens of the countries they live in is stark. India, for example, has 500 million unvaccinated people,2 one of the world’s highest numbers. Many of these unvaccinated people are the nation’s most marginalised (57% of the eligible population are fully vaccinated).1 In India, reliable data do not exist on the number of unvaccinated refugees as they are not accorded official status under Indian law…
<https://www.bmj.com/content/376/bmj.o703>

title: In-Hospital Mortality Disparities Among American Indian and Alaska Native, Black, and White Patients With COVID-19

jama network open | 30th march 2022

Question Are the higher in-hospital mortality rates for COVID-19 among American Indian and Alaska Native patients compared with other racial groups associated with differences in comorbidity burden?

Findings In this cross-sectional study of 18 731 US adults hospitalized with COVID-19 in 2020, American Indian and Alaska Native patients had a lower mean comorbidity risk score compared with the overall patient population, yet they were significantly more likely than patients of all other races to die in the hospital. Increased COVID-19 in-hospital deaths among American Indian and Alaska Native adults were not associated with increased comorbidity experiences in all populations.

Meaning These findings suggest that alternative factors contributing to disparate in-hospital mortality rates among Indigenous communities must be investigated further.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790506>

title: Racial Disparities in COVID-19 Outcomes Among Black and White Patients With Cancer

jama network open | 28th march 2022

Question Among patients with cancer and COVID-19, do non-Hispanic Black patients have more severe COVID-19 at presentation and worse COVID-19–related outcomes compared with non-Hispanic White patients, after adjusting for demographic and clinical risk factors?

Findings In this cohort study of 3506 patients, Black patients with cancer experienced significantly more severe COVID-19 outcomes compared with White patients with cancer, after adjustment for demographic and clinical risk factors.

Meaning These findings suggest that, within the framework of structural racism in the US, having cancer and COVID-19 is associated with worse outcomes among Black patients compared with White patients.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790424>

**title:** COVID-19 Booster Vaccination Among Individuals With Schizophrenia in Israel

jama psychiatry| 30th march 2022

Question Do individuals with schizophrenia receive the booster vaccination to the same extent as do individuals without schizophrenia?

Findings In this cohort study of 34 797 individuals with schizophrenia and matched controls, individuals with schizophrenia were less likely to be vaccinated with the COVID-19 booster vaccine, and gaps in vaccination remained the largest for the first vaccination. Time to reach vaccination was significantly longer for the group with schizophrenia but primarily with the first vaccine and to a smaller extent with the booster vaccine.

Meaning Study results suggest that for individuals with schizophrenia, the main barrier to COVID-19 vaccination was during the initiation phase.
<https://jamanetwork.com/journals/jamapsychiatry/article-abstract/2790725>

**international perspectives**

**title:** Covid-19: Americans who are over 50 or immunocompromised are advised to have second booster

bmj | 30th march 2022

Second booster doses against covid-19 for Americans aged over 50 and for certain immunocompromised people aged over 12, using either the Pfizer-BioNTech or the Moderna vaccine, may become available as early as later this week after they were authorised in the US.

The new recommendations from the Food and Drug Administration (FDA)1 and the Centers for Disease Control and Prevention (CDC)2 come as the BA.2 omicron variant spreads rapidly in the US and is responsible for about 55% of new infections. The variant seems to be more contagious but does not cause more severe infections. Peter Marks, director of the CDC’s Center for Biologics Evaluation and Research, said on 29 March, “Current evidence suggests some waning of protection over time against serious outcomes from covid-19 in older and immunocompromised individuals. Based on an analysis of emerging data, a second booster dose of either the Pfizer-BioNTech or Moderna covid-19 vaccine could help increase protection levels for these high risk individuals. “Additionally, the data show that an individual booster dose is critical in helping to protect all adults from the potentially severe outcomes of covid-19. So, those who have not received their initial booster dose are strongly encouraged to do so.”…
<https://www.bmj.com/content/376/bmj.o842>

**title:** Covid-19: US tracker overestimated deaths among children

BMJ | 29th march 2022

COVID-19 has amplified inequalities in global health and socioeconomic outcomes between HICs and
The US’s health protection agency has reduced the number of deaths it is attributing to covid-19 by more than 70 000 after what it referred to as “coding logic errors” were highlighted on social media. On 15 March the Centers for Disease Control and Prevention (CDC) removed 72 277 deaths, including those of 416 children, from its Covid-19 Data Tracker, which has been posting real time data collected from more than two dozen state health departments since April 2020.

The tracker is one of two sources used to report deaths from covid-19 in the US. The other is the National Center for Health Statistics’ website, which is also run by the CDC but relies on death certificates for its data. By mid-March the figures presented by the two sites differed substantially. For example, the Covid-19 Data Tracker put the number of deaths among infants and children aged 0-17 at 1700, while the statistics site stated 900…
<https://www.bmj.com/content/376/bmj.o831>

**title:** Covid-19: WHO set to reject Canadian plant based vaccine because of links with tobacco industry

BMJ | 28th MARCH 2022

COVID-19 has amplified inequalities in global health and socioeconomic outcomes between HICs and
A unique plant based coronavirus vaccine newly approved in Canada is unlikely to be listed for emergency use by the World Health Organization, a WHO official has warned, because a tobacco company is a major shareholder in the company that developed it.

Philip Morris Investments, a subsidiary of Marlboro cigarette manufacturer Philip Morris International, holds around one third of the equity in Medicago, a Quebec based vaccine maker. Medicago’s vaccine Covifenz, which uses virus like particles assembled from plant proteins, was approved by Health Canada on 24 February…
<https://www.bmj.com/content/376/bmj.o811>

**title:** Covid-19: Lockdowns spread in China as omicron tests “zero covid” strategy

BMJ | 31st march 2022

The force of the omicron BA.2 variant this week met the immovable object that is China’s zero covid policy as Shanghai locked down amid the country’s worst outbreak since early 2020. World oil prices fell and Indian drug manufacturers warned of ingredient shortages as the city responsible for 4% of China’s gross domestic product posted record case numbers on 30 March…
<https://www.bmj.com/content/376/bmj.o859>

**title:** How Japan survived covid-19

BMJ | 31st march 2022

The first peer-reviewed clinical trial evidence that a Covid-19 vaccine provided robust protection
The world’s third biggest economy seems to have emerged from the pandemic comparatively unscathed. Priyanka Borpujari speaks to health workers who survived the frontlines about how, and at what cost…
<https://www.bmj.com/content/376/bmj.o778>

**title:** Assessment of SARS-CoV-2 Mu Variant Emergence and Spread in Colombia

JAMA network open|30th march 2022

Widening gaps in global vaccine equity have led to a two-track pandemic with booster COVID-19

…To our knowledge, this is the first study to describe the molecular epidemiology of the Mu variant after it emerged in Colombia in 2021. The large number of cases during the study period is coincident with the introduction of the Mu variant; coupled with low vaccination coverage (45.5% by August, and high levels of SARS-CoV-2 antibody in the population4), this observation suggests that reinfection is likely common with the Mu variant. Previous studies have suggested that the Mu variant is resistant to convalescent and vaccine sera.5,6 The ability of the Mu variant to evade the immune response in vaccinated and previously infected individuals requires further study.

 Our study has some limitations. Because of the insufficient number of vaccinated persons in our study, we were unable to determine whether the Mu variant is more successful at evading resistance from vaccination compared with other variants. The observational nature of this study limits the generalizability of our findings, and the demographic, risk factor, and vaccination data were self-reported. Few persons were vaccinated at the time, and there were several vaccines in use in Colombia; thus, we were not able to assess the effectiveness of vaccination on the Mu variant.

Our data reflect the variant circulation in other populated regions of Colombia.6 With the introduction of the Delta and Omicron variants into the country, additional studies are needed to better understand the effect of the Mu variant.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790509>

We

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

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

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