COVID-19 weekly update

23rd May 2022

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**clinical management**

**title:** Severity and Incidence of Multisystem Inflammatory Syndrome in Children During 3 SARS-CoV-2 Pandemic Waves in Israel [research letter]

jama| 19th may 2022

Multisystem inflammatory syndrome in children (MIS-C) is a serious complication of SARS-CoV-2 infection.1 A previous study that described MIS-C cases in the first 3 waves of the COVID-19 pandemic found that the proportion of individuals with severe illness declined after the first wave.2 In Israel, the Omicron (B.1.1.529) variant started to spread in November 2021.3 We describe outcomes of MIS-C in a multicenter cohort and assessed incidence nationally during the Alpha, Delta, and Omicron variant waves…

…This study suggests that MIS-C during the Omicron wave was less severe than during the Alpha or Delta waves of the COVID-19 pandemic. Possible explanations include the Omicron variant itself, previous infection with SARS-CoV-2, vaccination against SARS-CoV-2, and improvement in treatment over time. In addition, the incidence rate of MIS-C during the Omicron wave was lower than during the Delta and Alpha waves. A 2022 study from South Africa on the Omicron wave reported no cases of MIS-C, a finding that corroborates these results.5 Limitations of the study include the small number of patients in the prospective cohort and the single-country data. Because MIS-C is a late-onset phenomenon of SARS-CoV-2 infection, cases that appeared after the 16-week period of each wave were not included.
<https://jamanetwork.com/journals/jama/fullarticle/2792718>

**title:** Association of Congenital and Acquired Cardiovascular Conditions With COVID-19 Severity Among Pediatric Patients in the US

jama | 17th may 2022

Question What is the association between individual congenital and acquired cardiovascular conditions and COVID-19 severity in pediatric patients?

Findings In this cohort study of 171 416 US individuals aged 2 months to 17 years with SARS-CoV-2 infection, cardiac arrest, cardiogenic shock, heart surgery, cardiopulmonary disease, heart failure, hypotension, nontraumatic cerebral hemorrhage, pericarditis, and biventricular defects were associated with increased COVID-19 severity.

Meaning The findings suggest that previous or preexisting cardiovascular conditions are associated with increased COVID-19 severity, in varying degrees, in pediatric patients.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2792374>

**title:** Acute hepatitis of unknown origin in children

BMJ| 17th may 2022

Many leads but few clear answers

Recent reports of severe acute hepatitis of unknown aetiology in previously healthy children across multiple countries have resulted in health alerts and a race to identify the underlying cause.

By 11 May, around 450 probable cases of acute hepatitis of unknown cause had been reported worldwide,1 with 163 in the UK by 3 May.2 Affected children were aged between 1 month and 16 years, although more than three quarters of those in the UK were under 5 years and those in the US had a median age of 2 years.2 Eleven children have died so far, and 31 have been reported to require liver transplants (11 in the UK, 5 in Europe, and 15 in the US).34 Gastrointestinal symptoms are common,245 including jaundice (71%), vomiting (63%), pale stools (50%), and diarrhoea (45%). Fever (31%) and respiratory symptoms (19%) are reported less often.6 Most affected children have not received a covid-19 vaccine.

Possible causes. Tests for hepatitis viruses A–E have been universally negative. Detailed laboratory investigation by the UK Health Security Agency (UKHSA) found that 91 of the 126 children (72%) tested for adenovirus had positive results, and adenovirus type 41f was identified in blood samples from all 18 children with successful subtype analysis.6 Adenovirus was also identified in 44% of stool samples and 29% of respiratory samples.6 Whole genome sequencing for adenovirus so far has been unsuccessful because of low viral loads and sample limitations.

Active SARS-CoV-2 infection has been confirmed in 24/132 (18%) of affected children in the UK, but serological testing is ongoing. Epstein-Barr virus, enterovirus, cytomegalovirus, respiratory syncytial virus, and human herpes viruses 6 and 7 have also been identified in UK patients, though at lower frequency. No common exposures have been identified.4567 Histopathology of explanted livers (n=6) or liver biopsy samples (n=8) from UK children showed variable severity, including hepatic necrosis. However, overall, pathology showed a non-specific pattern and no identifiable cause.

Working hypotheses. While adenovirus alone is rarely associated with fulminant hepatic failure in healthy children, other factors may increase vulnerability, so current hypotheses continue to include an adenovirus aetiology.46 According to the UKHSA, contributing factors may include abnormal susceptibility or host response—for instance, because of lack of previous exposure; increased community prevalence of adenovirus; or abnormal susceptibility because of priming by previous infection, co-infection with SARS-CoV-2 or other pathogens, or toxin, drug, or environmental exposure.

Other leading hypotheses include a post-infectious SARS-CoV-2 syndrome, a new variant of adenovirus, non-infectious causes, a novel pathogen, or a new variant of SARS-CoV-2.

Covid-19 associated hepatitis in children was reported in 37 children two to six weeks after SARS-CoV-2 infection during an outbreak of the delta variant in India.9 The children’s synthetic liver function was unaffected with no jaundice; none had fulminant liver failure; and there were no deaths. While transient transaminitis without jaundice is common in children with other viral infections, the recent cases of hepatitis seem more severe than covid associated hepatitis. Still, the current outbreak may represent the more severe end of the spectrum of this condition, or perhaps another post-infectious inflammatory or autoimmune syndrome.

Children in a recent series of cases from Alabama had no history of SARS-CoV-2 infection, and although all tested positive for adenovirus, liver biopsy samples showed no viral inclusions and no evidence of adenovirus infected hepatic tissue or viral particles.5 Histopathology findings remain hard to interpret during fulminant hepatic failure because of necrosis in the liver biopsy sample. However, no pattern of necrosis or apoptosis consistent with known causes of viral hepatitis has emerged. Histopathology results from a larger patient cohort would provide additional insights.

Non-infectious or toxicological causes have not been identified but cannot be entirely ruled out just yet. Previous SARS-CoV-2 infection causing an immunopathological response that leads to more severe adenovirus infection is also being considered and requires further investigation. Case-control analyses of serology would be helpful to identify a true signal.6 According to the UKHSA report, 75% of children with available data had been given paracetamol, all within therapeutic range, and 70% had been exposed to dogs, though the significance of both remains unclear.6 Previous investigations of children with acute liver failure of unknown origin reported concurrent infections with multiple viruses.10 In the current outbreak, children had evidence of infection with a variety of other common respiratory and gastrointestinal viral pathogens.567 Identifying the causal agent or agents may be challenging, and previous efforts to use next generation sequencing to detect viruses have not always been successful.

This seemingly rare but severe condition is likely to have a complex pathology. While the cause or causes remain unknown, and agent specific control measures cannot be identified, adherence to general risk mitigation and infection control strategies are important. Risks assessments should consider all potential causative agents. Outbreak investigation is a well trodden path: a methodical and empirical approach using standardised case definitions and diagnostic algorithms coupled with an open mind, information sharing, and collaboration will help facilitate the global response.
<https://www.bmj.com/content/377/bmj.o1197>

**long-term effects**

**title:** Are vaccines a potential treatment for long covid?

BMJ| 18th may 2022

Benefits are possible, but we need more evidence and a mechanism of action

Vaccines in the covid-19 pandemic have been a game changer in reducing rates of SARS-CoV-2 infection and hospital admission for, and death with, covid-19. They also reduce the chance of developing long covid by about half among people who are vaccinated before they develop covid-19.1 However, the effect of vaccines for people who already have long covid is a contentious area for both patients and healthcare professionals. In a linked paper, Ayoubkhani and colleagues (doi:10.1136/bmj-2021-069676) report findings from the largest published study on this topic to date.2 From a random sample of the UK population, they identified 28 356 adults (18-69 years) who were vaccinated after a positive SARS-CoV-2 test result, of whom 6729 (23.7%) reported long covid symptoms (>12 weeks) of any severity at least once during follow-up. Participants were followed for seven months to determine the relationship between vaccination, long covid, and symptom profiles after the first and second dose of either an adenovirus vector or mRNA vaccine.2

In an interrupted time series model adjusting for prespecified covariates, the authors found a 12.8% reduction in the odds of reporting long covid immediately after the first vaccine dose, but this reduction was not sustained over the following 12 weeks. However, an 8.8% reduction in the odds of long covid after a second dose was sustained over the next nine weeks. The authors suggested inadequate immune response as a reason for lack of sustained effect after the first dose…
<https://www.bmj.com/content/377/bmj.o988>

title: SARS-COV-2 RNA CAN PERSIST IN STOOL MONTHS AFTER RESPIRATORY TRACT CLEARS VIRUS

JAMA| 18th may 2022

SARS-CoV-2, or at least pieces of it, sticks around longer in some infected individuals than respiratory sample testing would suggest, a recent study found. After respiratory samples tested negative, a small proportion of the 113 study participants continued to shed SARS-CoV-2 RNA in their feces—about 4% of them for at least 7 months—and those people were more likely to report ongoing gastrointestinal (GI) symptoms, researchers reported in the journal Med.

The findings provide more evidence that SARS-CoV-2 infects the gut as well as the lungs and could help explain why some people with “long COVID” have persistent abdominal pain, nausea, and other GI symptoms, according to the authors…
<https://jamanetwork.com/journals/jama/fullarticle/2792688>

**title:** Trajectory of long covid symptoms after covid-19 vaccination: community based cohort study

BMJ| 18th may 2022

Objective To estimate associations between covid-19 vaccination and long covid symptoms in adults with SARS-CoV-2 infection before vaccination.

Design Observational cohort study.

Setting Community dwelling population, UK.

Participants 28 356 participants in the Office for National Statistics COVID-19 Infection Survey aged 18-69 years who received at least one dose of an adenovirus vector or mRNA covid-19 vaccine after testing positive for SARS-CoV-2 infection.

Main outcome measure Presence of long covid symptoms at least 12 weeks after infection over the follow-up period 3 February to 5 September 2021.

Results Mean age of participants was 46 years, 55.6% (n=15 760) were women, and 88.7% (n=25 141) were of white ethnicity. Median follow-up was 141 days from first vaccination (among all participants) and 67 days from second vaccination (83.8% of participants). 6729 participants (23.7%) reported long covid symptoms of any severity at least once during follow-up. A first vaccine dose was associated with an initial 12.8% decrease (95% confidence interval −18.6% to −6.6%, P<0.001) in the odds of long covid, with subsequent data compatible with both increases and decreases in the trajectory (0.3% per week, 95% confidence interval −0.6% to 1.2% per week, P=0.51). A second dose was associated with an initial 8.8% decrease (95% confidence interval −14.1% to −3.1%, P=0.003) in the odds of long covid, with a subsequent decrease by 0.8% per week (−1.2% to −0.4% per week, P<0.001). Heterogeneity was not found in associations between vaccination and long covid by sociodemographic characteristics, health status, hospital admission with acute covid-19, vaccine type (adenovirus vector or mRNA), or duration from SARS-CoV-2 infection to vaccination.

Conclusions The likelihood of long covid symptoms was observed to decrease after covid-19 vaccination and evidence suggested sustained improvement after a second dose, at least over the median follow-up of 67 days. Vaccination may contribute to a reduction in the population health burden of long covid, although longer follow-up is needed.
<https://www.bmj.com/content/377/bmj-2021-069676>

**title:** Identifying who has long COVID in the USA: a machine learning approach using N3C data

the lancet digital health| 16th may 2022

Post-acute sequelae of SARS-CoV-2 infection, known as long COVID, have severely affected recovery from the COVID-19 pandemic for patients and society alike. Long COVID is characterised by evolving, heterogeneous symptoms, making it challenging to derive an unambiguous definition. Studies of electronic health records are a crucial element of the US National Institutes of Health's RECOVER Initiative, which is addressing the urgent need to understand long COVID, identify treatments, and accurately identify who has it—the latter is the aim of this study…
[https://www.thelancet.com/journals/landig/article/PIIS2589-7500(22)00048-6/fulltext](https://www.thelancet.com/journals/landig/article/PIIS2589-7500%2822%2900048-6/fulltext)

**rates and variants**

**title:** Clinical severity of COVID-19 in patients admitted to hospital during the omicron wave in South Africa: a retrospective observational study

the lancet global health| 18th may 2022

Up to the end of January, 2022, South Africa has had four recognisable COVID-19 pandemic waves, each predominantly dominated by one variant of concern: the ancestral strain with an Asp614Gly mutation during the first wave, the beta variant (B.1.351) during the second wave, the delta variant (B.1.617.2) during the third wave, and lastly, the omicron variant (B.1.1.529) during the fourth wave. We aimed to assess the clinical disease severity of patients admitted to hospital with SARS-CoV-2 infection during the omicron wave and compare the findings with those of the preceding three pandemic waves in South Africa…
[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00114-0/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X%2822%2900114-0/fulltext)

**title:** Decoding the next SARS-CoV-2 variant

the lancet global health| 18th may 2022

What will the next SARS-CoV-2 variant bring to the world? Much mental horsepower has been dedicated to this question, ever since it became apparent in mid-2020 that the virus was far from settled into a stable evolutionary niche. The selection pressure on a virus is to generate as many onward infections as possible, whether through changes in its intrinsic transmissibility or through immune evasion. Sure enough, subsequent variants of concern have increased one or both parameters, with more recent variants being both more contagious and far better at evading antibody-driven responses from vaccines and earlier infection waves. The process has shown little evidence of slowing either, leading commentators to wonder aloud about the prudence of choosing the Greek alphabet, which contains only 24 letters, to name variants.

A rapid uptick in COVID-19 cases in southern Africa in November, 2021—caused by the variant B.1.1.529, subsequently named omicron by WHO—in turn drove a rapid global surge in cases. The race was then on to work out what the clinical impact of the new variant was likely to be. Virulence is not a primary focus of natural selection, just its by-product, and is thus complex to predict. SARS-CoV-2 had already disproven the comforting, but evolutionary naive, myth that respiratory viruses inevitably evolve towards lesser virulence—the alpha (B.1.1.7), beta (B.1.351), and delta (B.1.617.2) variants had instead proven to be a ghastly sequence of ever-worsening intrinsic virulence. What would omicron bring?
[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00199-1/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X%2822%2900199-1/fulltext)

**infection control**

title: First Breathalyzer Test to Diagnose COVID-19

jama|17th may 2022

The first test that uses breath samples to diagnose COVID-19 recently received Emergency Use Authorization from the FDA. The InspectIR COVID-19 Breathalyzer, which uses an instrument about the size of a piece of carry-on luggage—a “chemical-lab-in-a-box,” as its developer describes it—can provide results within 3 minutes, according to the FDA. Testing with the device is performed by specially trained operators under the supervision of a health care professional licensed to prescribe tests in physicians’ offices, hospitals, and mobile testing sites.

 A study involving 2409 people, only some with COVID-19 symptoms, validated the performance of the testing device. In the study, the breathalyzer correctly identified 91.2% of positive samples and 99.3% of negative samples, according to the FDA, which noted that a follow-up clinical study found the test performed with similar sensitivity with the Omicron variant.

The breathalyzer uses gas chromatography–mass spectrometry to detect 5 volatile organic compounds (VOCs) in exhaled breath that are associated with SARS-CoV-2 infection, according to the FDA. When those VOCs are detected, the test result should be confirmed with a molecular test. Negative test results from the breathalyzer don’t rule out SARS-CoV-2 infection and should be considered in the context of the patient’s recent exposures, history, and symptoms consistent with COVID-19, FDA officials noted…
<https://jamanetwork.com/journals/jama/fullarticle/2792268>

**title:** Omicron BA.1/1.1 SARS-CoV-2 Infection among Vaccinated Canadian Adults

new england journal of medicine| 18th may 2022

The incidence of the omicron BA.1/1.1 variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which rapidly spread worldwide even among vaccinated persons, is incompletely defined.1 We quantified the incidence of SARS-CoV-2 infection during the initial omicron BA.1/1.1 variant wave among Canadian adults2 and the contribution of previous infection and concurrent vaccination to age-specific active immunity…
<https://www.nejm.org/doi/full/10.1056/NEJMc2202879?query=featured_coronavirus>

**title:** NICE publishes guidance to increase uptake of routine vaccinations

BMJ | 20th may 2022

GP practices and other providers of healthcare services should have a named vaccination lead in order to increase uptake of routine vaccinations, according to new guidance from the National Institute for Health and Care Excellence.1

The guideline, Vaccine uptake in the general population, says the vaccination lead should be responsible for identifying people eligible for vaccination, keeping records up to date, and sending out appointments and reminders.

GP practices should update vaccine records within two weeks and validate their vaccination records at least monthly against data sources received, the guideline says. It adds that the vaccination lead should also help to identify those who are housebound and are less likely to be vaccinated because they cannot attend appointments or vaccination clinics.
<https://www.bmj.com/content/377/bmj.o1260.full>

**title:** Covid-19: JCVI advises further booster for vulnerable adults and health and care workers

BMJ |20th MAY 2022

An additional booster dose of covid-19 vaccine will be offered to the most vulnerable adults and some health and social care workers this autumn, under draft guidance from the Joint Committee on Vaccination and Immunisation. However, most people in the UK under the age of 65 will be excluded from the autumn booster programme if the interim advice, which has been issued for “purposes of operational planning,” remains in place. The JCVI said that considerable uncertainty remained over the likelihood, timing, and severity of any potential future wave of covid in the UK in the year ahead. Despite this uncertainty, winter will remain the season when the threat from covid is greatest for individuals and for healthcare workers, it said.

The committee added that the primary objective of the 2022 autumn booster programme would be to increase population immunity and protection against severe covid disease, specifically hospital admissions and deaths, over the winter period. It recommended that in autumn 2022, a further covid vaccine should be offered to:

•-Residents and staff of care homes for older adults
•-“Frontline” health and social care workers
•-All those 65 years of age or over, and
•-Adults aged 16-64 years who are in a clinical risk group.

Currently a narrower group is being offered a spring booster: the over 75s, residents in care homes for older adults, and people aged 12 or over who are immunosuppressed. Wei Shen Lim, chair of covid-19 vaccination on the JCVI, said, “Last year’s autumn booster vaccination programme provided excellent protection against severe covid-19, including against the omicron variant. We have provided interim advice on an autumn booster programme for 2022 so that the NHS and care homes are able to start the necessary operational planning, to enable high levels of protection for more vulnerable individuals and frontline healthcare staff over next winter.”

The JCVI said it will continue to review the vaccination programme and the epidemiological situation, particularly in relation to the timing and value of doses for less vulnerable older adults and those in clinical risk groups, ahead of autumn 2022. Final plans, including further detail on the definitions of clinical risk groups, will be published in due course.

Commenting on the advice, Jonathan Ball, professor of molecular virology at the University of Nottingham said, “We know that immunity to covid-19 following vaccination or indeed infection contracts over time, so giving those individuals most at risk from developing severe covid-19 a boost just before virus circulation is likely to pick up during autumn and winter months seems sensible.” But Ball added, “The exact timing will be important, as you don't want to wait until virus circulation has already started to increase, although hopefully those most at risk have already had their spring booster, which will be standing them in good stead.”

However, Christina Pagel, professor of operational research at University College London and a member of the Independent SAGE group, commented on Twitter. “What this means is that JCVI has effectively given up on trying to prevent infections and that will have consequences (bad ones) for long covid.”

Meanwhile, in the US, the Centers for Disease Control has recommended vaccine boosters for children aged 5 to 11 years. Boosters were recommended for adults in November and for children 12 or older in January.
<https://www.bmj.com/content/377/bmj.o1277>

**title:** Covid-19: Second boosters may benefit at-risk groups but have “minimal” impact for others, says WHO

BMJ| 19th may 2022

Short term benefits are seen after a second covid-19 vaccine booster—normally a fourth vaccine dose—in health workers, over 60s, and people with immunocompromising conditions, the World Health Organization has said. But early data show that the benefit may be “minimal” in healthy younger populations, it added. WHO said that evidence on the usefulness of these doses in all groups was sparse, with studies available only for mRNA vaccines such as the Pfizer-BioNTech and Moderna vaccines.

WHO’s evidence review included seven studies, six of which were conducted in Israel and one in Canada. Six of the studies evaluated the relative effectiveness of a fourth dose four months after a third dose of mRNA vaccine, compared with people who received three doses. The other study provided data on absolute vaccine effectiveness, comparing the fourth dose schedule with unvaccinated people. The maximum follow-up in the available studies was short, ranging from two to 10 weeks after the fourth dose. The studies reported a variety of outcomes, including that a fourth dose reduced the number of breakthrough infections in healthcare workers and that a fourth dose led to slightly higher antibody levels than those achieved after a third dose…
<https://www.bmj.com/content/377/bmj.o1259>

**title:** VACCINATION PLUS PREVIOUS INFECTION: PROTECTION DURING THE OMICRON WAVE IN BRAZIL

the lancet infectious diseases| 16th may 2022

As of May 11, 2022, an estimated 519 million individuals have been infected with SARS-CoV-2, and at least 11 billion COVID-19 vaccine doses have been administered worldwide. Therefore, understanding hybrid immunity (ie, immunity derived from infection plus vaccination) is crucial to guide future vaccination policies. We found that vaccination provided additional protection to that induced by past infection during the gamma (P.1) and delta (B.1.617.2) variant waves of the pandemic in Brazil. With the emergence of the omicron (B.1.1.529) variant, vaccine effectiveness appears to decay, but protection in individuals who have been previously infected and vaccinated remains unknown. We analysed the effect of hybrid immunity in preventing infection and severe outcomes during circulation of the omicron variant in Brazil…
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00288-2/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900288-2/fulltext)

**title:** Safety and immunogenicity of heterologous boost immunisation with an orally administered aerosolised Ad5-nCoV after two-dose priming with an inactivated SARS-CoV-2 vaccine in Chinese adults: a randomised, open-label, single-centre trial

the lancet respiratory medicine| 20TH MAY 2022

Due to waning immunity and protection against infection with SARS-CoV-2, a third dose of a homologous or heterologous COVID-19 vaccine has been proposed by health agencies for individuals who were previously primed with two doses of an inactivated COVID-19 vaccine.

Methods We did a randomised, open-label, controlled trial to evaluate the safety and immunogenicity of heterologous boost immunisation with an orally administered aerosolised adenovirus type-5 vector-based COVID-19 vaccine (Ad5-nCoV) in Chinese adults (≥18 years old) who had previously received two doses of an inactivated SARS-CoV-2 vaccine—Sinovac CoronaVac. Eligible participants were randomly assigned (1:1:1) to receive a heterologous booster vaccination with a low dose (1·0 × 1011 viral particles per mL; 0·1 mL; low dose group), or a high dose (1·0 × 1011 viral particles per mL; 0·2 mL; high dose group) aerosolised Ad5-nCoV, or a homologous intramuscular vaccination with CoronaVac (0·5 mL). Only laboratory staff were masked to group assignment. The primary endpoint for safety was the incidence of adverse reactions within 14 days after the booster dose. The primary endpoint for immunogenicity was the geometric mean titres (GMTs) of serum neutralising antibodies (NAbs) against live SARS-CoV-2 virus 14 days after the booster dose. This study was registered with ClinicalTrials.gov, NCT05043259.

Findings Between Sept 14 and 16, 2021, 420 participants were enrolled: 140 (33%) participants per group. Adverse reactions were reported by 26 (19%) participants in the low dose group and 33 (24%) in the high dose group within 14 days after the booster vaccination, significantly less than the 54 (39%) participants in the CoronaVac group (p<0·0001). The low dose group had a serum NAb GMT of 744·4 (95% CI 520·1–1065·6) and the high dose group had a GMT of 714·1 (479·4–1063·7) 14 days after booster dose, significantly higher than the GMT in the CoronaVac group (78·5 [60·5–101·7]; p<0·0001).

Interpretation We found that a heterologous booster vaccine with an orally administered aerosolised Ad5-nCoV is safe and highly immunogenic in adults who have previously received two doses of CoronaVac as the primary series vaccination.
[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00087-X/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600%2822%2900087-X/fulltext)

**title:** Neutralization of the SARS-CoV-2 Deltacron and BA.3 Variants

NEW ENGLAND JOURNAL OF MEDICINE| 18TH MAY 2022

…Overall, our results indicate that BA.3 is not a substantial immune-escape variant, a finding that is likely due to its reduced number of mutations in the receptor-binding domain as compared with the BA.1 and BA.2 variants. However, the deltacron variant retains the strong resistance of other omicron sublineages and has no enhanced sensitivity to serum obtained during the delta wave. Although the effect of the delta-derived spike mutations in the N-terminal domain on virus replication and pathogenesis remains unclear, these mutations do not appear to impair neutralization resistance. Recombination of SARS-CoV-2 variants and the potential emergence of a more virulent variant with strong immune escape remains a critical concern and requires ongoing monitoring.
<https://www.nejm.org/doi/full/10.1056/NEJMc2205019?query=featured_coronavirus>

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

new engand journal of medicine | 19th May2022

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…

…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>

**title:** Safety and Efficacy of a Third Dose of BNT162b2 Covid-19 Vaccine

new england journal of medicine | 19th may 2022

Active immunization with the BNT162b2 vaccine (Pfizer–BioNTech) has been a critical mitigation tool against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during the coronavirus disease 2019 (Covid-19) pandemic. In light of reports of waning protection occurring 6 months after the primary two-dose vaccine series, data are needed on the safety and efficacy of offering a third (booster) dose in persons 16 years of age or older…

…A third dose of the BNT162b2 vaccine administered a median of 10.8 months after the second dose provided 95.3% efficacy against Covid-19 as compared with two doses of the BNT162b2 vaccine during a median follow-up of 2.5 months.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2200674>

**title:** Demographic and Clinical Factors Associated With Anti–SARS-CoV-2 Antibody Levels After 2 BNT162b2 mRNA Vaccine Doses

JAMA network open | 19th MAY 2022

Question What factors are associated with serum levels of anti–SARS-CoV-2 antibodies after COVID-19 vaccination in healthy young and middle-aged persons at 6 months?

Findings In this cohort study of 50 individuals, anti–SARS-CoV-2–specific antibody levels at 2, 4, and 6 months after COVID-19 vaccination were inversely correlated with body weight. Young and middle-aged healthy adults weighing less than 55 kg maintained a high antibody level 6 months after the second dose of BNT162b2 vaccination.

Meaning In this study, the inverse correlation of anti–SARS-CoV-2–specific antibody levels with weight was sustained up to 6 months after vaccination; further studies are needed to clarify the antibody cutoff level to protect individuals from severe infection.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2792387>

**title:** Routine Surveillance and Vaccination on a University Campus During the Spread of the SARS-CoV-2 Omicron Variant

JAMA network open | 18th may 2022

Subtle variations in immune responses to the mRNA-1273 (Moderna) and BNT162b2 (Pfizer-
As SARS-CoV-2 was detected in the US, emergency public health measures took effect, including shutting down schools.1 As prevention and control measures improved, emergency response policies were rolled back.1 Cornell University opened for residential instruction in Fall 2021 using an extensive testing, contact tracing, and isolation program in partnership with the Tompkins County Health Department (Table).2 Vaccination was mandated for all students and encouraged for employees. Masks were required on-campus, and isolation orders and contact tracing occurred within hours of any positive result. We hypothesized that these measures would limit COVID-19 spread on campus and sought to monitor this with a case-series study of university testing records…

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<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2792382>

**HEALTH MANGEMENT & workforce well-being**

**title:** British Medical Association Covid Review

BMA| 19th may 2022

The BMA have undertaken a review into the UK Government’s handling of the pandemic and its impact on the NHS, the health of the population, and doctors. These reports conclude that the UK Government failed in its duty of care to protect doctors and the wider healthcare workforce from avoidable harm and suffering in its management of the Covid-19 pandemic.
<https://kingsfund.blogs.com/health_management/2022/05/british-medical-association-covid-review.html>

**title:** Covid-19: Government failed to protect doctors during pandemic, BMA inquiry finds

BMJ | 19th may 2022

The recent changes to covid-19 restrictions indicate a new phase of the pandemic, where we are
The UK government failed in its duty of care to protect doctors and other healthcare staff from avoidable harm and suffering in its management of the covid-19 pandemic, a major review by the BMA has concluded.

Two reports12 published on 19 May document the experiences of thousands of UK doctors throughout the pandemic, drawing on real time surveys carried out over the past two years, formal testimonies, data, and evidence sessions. The reports will form part of a wider review by the BMA into the government’s handling of the pandemic, with three further instalments to come.

The evidence lays bare the devastating impact of the pandemic on doctors and the NHS, with repeated mistakes, errors of judgment, and failures of government policy amounting to a failure of a duty of care to the workforce, the BMA said.

Chaand Nagpaul, BMA chair of council, said, “A moral duty of government is to protect its own healthcare workers from harm in the course of duty, as they serve and protect the nation’s health. Yet, in reality, doctors were desperately let down by the UK government’s failure to adequately prepare for the pandemic, and their subsequent flawed decision making, with tragic consequences.

“The evidence presented in our reports demonstrates, unequivocally, that the UK government failed in its duty of care to the medical profession.”

Burnout and distress

Testimonies from doctors reveal fears and anxieties about shortages of personal protective equipment (PPE) and a lack of risk assessments and show that the pandemic seriously affected their mental and physical health.

“Many doctors were left unprotected due to critical shortages of PPE as coronavirus hit our shores, resulting in healthcare professionals becoming infected at a higher rate than the rest of the population,” said Nagpaul. “Hundreds of healthcare workers lost their lives after contracting covid-19. And 95% of doctors who died in April 2020 were from an ethnic minority, a figure which demands that the UK government addresses the deep race inequalities afflicting our NHS workforce.”

The reports, which will form part of the BMA’s submission to the upcoming UK covid-19 public inquiry, also highlight the burnout, overwork, distress, trauma, and isolation that doctors endured from working during the pandemic.

They also make key recommendations for improving future pandemic preparedness, such as addressing the “chronic underinvestment” in services that left the UK ill prepared for tackling covid. Attention should be paid to ensuring sufficient levels of PPE, testing, public health capacity, and staffing to handle future crises, they advised.

Nagpaul added, “The lessons from this review need to be learnt and acted on now—given that new variants, new viruses, or future surges of demand can happen swiftly. We must never see a repeat of doctors and healthcare workers left exposed and vulnerable, and we can never afford to see another disaster on this scale ever again.”
<https://www.bmj.com/content/377/bmj.o1235>

**title:** David Oliver: Protecting healthcare workers in future pandemics

BMJ | 18th may 2022

Early in the pandemic, neither the NHS’s clinical or ancillary staff nor social care workers were adequately protected from the risks of catching covid-19 in the course of their work. In the UK alone, hundreds of infected workers have died, thousands have been admitted to hospital, and tens of thousands have experienced long term effects.123 How do we improve staff protection next time? Here’s my manifesto.

We should ensure sufficient stockpiles of PPE throughout an outbreak, with adequate supply lines from trusted providers of high specification equipment. The contracting should be open and transparent, and due diligence should be applied in tendering.

Before covid, our government had carried out pandemic preparedness exercises and then ignored the recommendations.4 Several other countries had sufficient PPE reserves for years, not months. We had left things to chance.56 And then, in desperation, we placed numerous public contracts with PPE suppliers, some providing substandard or unusable PPE. Some had financial or personal links to government ministers.

Those in charge of infection control and health protection advice in national bodies need to be more responsive and flexible in response to the changing evidence. In the first months of the pandemic the UK departed from the World Health Organization’s guidance on PPE specification and downgraded the requirements. Basic surgical masks were said to offer sufficient protection in clinical work not involving aerosol generating procedures (AGPs) such as mechanical ventilation—generally in critical care and high dependency areas. Concerns were raised that equipment shortages, not data, might be driving decisions.7

Research data subsequently showed that workers looking after covid patients in other ward areas without AGPs were far more likely to develop severe covid infection than other staff groups,8 that covid had a partially airborne route of transmission, and that better building ventilation was an important protective measure.91011 Higher specifications of protective masks could have been recommended, but the guidelines were slow to reflect this.

Staff members need individualised risk assessments incorporating their underlying health, their age, sex, and ethnicity, and their previous infection and vaccination status. Details should be noted of the clinical area they work in, and they should be fitted for masks that are reliably available for use. This didn’t happen consistently despite commitments from NHS Employers.1213

The concerns of staff who are putting their own health on the line shouldn’t be ignored. Surely it’s reasonable for the precautionary principle to be applied, even if it means supplying PPE of a higher specification than is technically indicated? Too often, staff who raised concerns or wore higher grade PPE were silenced or warned off.1415

We should be more open to learning from cases of staff becoming infected, admitted to hospital, or dying in the course of their work. My news investigation in The BMJ on the issue of staff PPE prompted obfuscation and denial from official bodies, while government communication teams and ministers repeatedly played down the subject of staff protection.16 This is the antithesis of an open culture and a learning organisation.

We must no longer allow social care to be treated as an afterthought—specifically, workers in care homes or clients’ own homes, or even community and primary healthcare staff—while PPE is preferentially supplied to hospitals.17 Everyone in hands-on caring and clinical roles deserves sufficient protection. We should ensure adequate, rapid access to free infection testing for staff in direct contact roles. This hasn’t always been present.1819

Finally, England’s health and social care secretary, who is not a clinician or an operational manager, should not be ordering hospitals (as was recently reported) to ask them to over-ride their own local risk assessments and policies on infection control to help them meet politically motivated imperatives.2021

Let’s see a clear set of commitments to such actions from the government and its agencies, rather than waiting for reports to appear. The next pandemic could be around the corner.
<https://www.bmj.com/content/377/bmj.o1200>

**title:** Understanding The Distinct Challenges For Nurses In Care Homes: Learning From Covid-19 To Support Resilience And Mental Wellbeing

university of east anglia |20th may 2022

This THRIVE research aims to understand Nursing and Midwifery Council registered nurses’ experiences of working in care homes for older people during the Covid-19 pandemic, how this impacted on resilience, mental health and wellbeing, and to collaboratively develop theory-informed approaches for ongoing and future support. The report makes six recommendations to support care home nurses to recover from the pandemic and plan for future major events.
<https://kingsfund.blogs.com/health_management/2022/05/understanding-the-distinct-challenges-for-nurses-in-care-homes-learning-from-covid-19-to-support-res.html>

**title:** IMPACT OF COVID-19 ON FERTILITY TREATMENT 2020

Human Fertilisation & Embryology Authority (HFEA) |20th may 2022

This report looks at changes in UK fertility treatment during the Covid-19 pandemic, including treatment numbers, funding, and donation. The report reveals that NHS-funded IVF treatments fell by seven per cent across the UK (35 per cent, 2019 to 28 per cent, 2020), with almost 26,000 patients over 35 receiving IVF treatments; a group prioritised by clinics as the chance of having a baby following fertility treatment decreases with age. The HFEA say this latest data confirms that fewer patients experienced delays during the pandemic than initially feared. This actually shows, a very small drop in treatments given the far-reaching impact of the pandemic across healthcare.
<https://kingsfund.blogs.com/health_management/2022/05/impact-of-covid-19-on-fertility-treatment-2020.html>

**recovery**

**title:** Effective post-pandemic governance must focus on shared challenges

the lancet| 16th may 2022

…We previously speculated that the unexpected increase in childhood cancer incidence rates in
The COVID-19 pandemic has highlighted profound weaknesses in the global governance of health; inadequate preparation, coordination, and accountability hampered the collective response of nations at each stage. Changes to the global health architecture are necessary to mitigate the health and socioeconomic damage of the ongoing pandemic, and to prepare for the next major global threat to health. Against this backdrop, on April 4, 2022, the London School of Economics and Political Science, London, UK, hosted a meeting on the topic, “Paying the Pandemic Piper: Global Health and Economic Security”. The cross-sectoral stakeholders who participated at the meeting arrived at several insights, including the key proposals captured here. We recommend international institutions focus on their core missions and unique capabilities to respond to global externalities—ie, policy areas and challenges where the actions or inaction of any one country affect all global actors…
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00891-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2900891-1/fulltext)

**title:** Pandemic treaty: a chance to level up on equity

BMJ | 20th may 2022

The Intergovernmental Negotiating Body (INB) is in the midst of developing a blueprint for the proposed pandemic instrument: a political framework to prevent, detect, and respond to emerging infectious diseases and pandemics in the future. While the International Health Regulations 2005 (IHR) already exist to govern this transnational challenge, it has proven insufficient for government compliance during covid-19 where we have seen widespread contraventions of the obligations placed on states.1 Such contraventions have in turn contributed to the scale of the spread of covid-19 globally. Consequently, some governments have championed the idea of a pandemic instrument to ensure political commitment and adherence to public health and evidence based recommendations, know how and international legal requirements.23

One of the key principles which has underscored the pandemic instrument discussions—at the World Health Assembly Special Session, the 150th World Health Organisation Executive Board Meeting, and the INB’s public hearings—has been that of equity. Yet, in practice equity has not been related to access to and distribution of medical countermeasures, such as vaccines, in future pandemics.4 The failures of the patent based system and advance market commitments has undermined the success of global public goods approach such as COVAX. Many states, particularly those low and middle income countries that have suffered from being unable to purchase covid-19 vaccines, are demanding that equitable access and distribution is included into the pandemic instrument…
<https://www.bmj.com/content/377/bmj.o1279>

**title:** Effective post-pandemic governance must focus on shared challenges

the lancet| 16th may 2022

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**title:** Transforming or tinkering: the world remains unprepared for the next pandemic threat

the lancet| 18th may 2022

…This COVID-19 crisis has weakened the ability of countries to withstand additional global shocks. The combined impacts of the pandemic, the Russian invasion of Ukraine, and increasing inflation in many countries are estimated to push up to 95 million more people into poverty in 2022 compared with pre-pandemic projections. The consequences of not ending the acuity of this pandemic are more illness and death, health systems stretched to the limit, deepening social divisions, widening economic inequalities, and further losses to individual households.

In the Independent Panel for Pandemic Preparedness and Response's 1-year progress report, Transforming or Tinkering? Inaction Lays the Groundwork for Another Pandemic, published on May 18, 2022, we set out these grim tolls as reasons to make concerted efforts to end the harms of COVID-19 and transform systems through actions that are well within the collective capacity of governments and global agencies. Containing pandemic threats is a choice. Through fragmented and slow processes, the world is choosing to risk a repeat of the events that resulted in the current situation.

To produce key evidence for the 1-year progress report, we consulted with civil society, received 50 responses to a survey from 24 countries, held two academic round tables, and did a systematic review of the literature. There was broad support for the recommendations of the Independent Panel for Pandemic Preparedness and Response, and after more than 2 years of learning, broader themes were also emphasised: the case for preventing pandemic threats upstream; the centrality of human rights, investing in communities, and maintaining trust; the need for regional self-sufficiency; the need to address inequalities and the social determinants of health; and the results of neglecting to invest in promoting healthy populations…
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00929-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2900929-1/fulltext)

**title:** Offline: How to fix pandemic preparedness

the lancet |21st MAY 2022

Surveillance. Detection. Response. The elements of a robust public health system to prevent the next (inevitable) pandemic are well understood. An early warning system for pneumonias of unknown aetiology is of paramount importance. Debates abound about how to deliver these crucial functions. A pandemic treaty. Revisions to the International Health Regulations. The role of WHO. Financing instruments. Workforce. There is little consensus. The sad truth is that political disagreements will tie these questions up in the mucilaginous bureaucracy that is today's global health. But if countries wanted to act now, if they wanted to avoid waiting for the cumbersome machinery of international diplomacy to grind out a suboptimal compromise, there is something they could do to diminish the impact of a new pandemic—attack, control, and defeat non-communicable diseases (NCDs)…
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00928-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2900928-X/fulltext)

**title:** States cannot negotiate a pandemic treaty alone

BMJ | 14th may 2022

Two years after SARS-COV-2 was declared a public health emergency, global estimates of excess
Global cooperation in response to the covid-19 pandemic has failed. Despite an established World Health Organisation (WHO) framework for early outbreak responses—the International Health Regulations, which require states to implement pathogen surveillance, detection, and alerts, and accurate public health communications—most states were sluggish and uncoordinated in their collective responses to covid-19. Future state negotiations to develop a pandemic treaty must look to civil society participation as a human rights and public health imperative.

States have remained divided in their response to covid-19 which has risked and likely cost millions of lives. The virus has deepened economic woes, exposing and worsening social disparities that disproportionately impact on marginalised and disadvantaged people, had dire impact on the physical and mental health of overburdened health workers, and exacerbated gender inequalities. State responses to the pandemic have resulted in a parallel “pandemic of human rights abuses.”1

It is in this context that the World Health Assembly accepted a recommendation to negotiate and draft a pandemic treaty.2 It is down to member states of the WHO—comprising nearly all the countries in the world—to adopt the treaty, but government representatives alone will not be able to draft an adequate instrument to prevent failed responses to future pandemics…
<https://www.bmj.com/content/377/bmj.o1281>

**public health & health inequalities**

**title:** Covid-19: Sexually transmitted diseases surged in US during pandemic

BMJ | 20th may 2022

US cases of gonorrhoea, syphilis, and congenital syphilis declined at the beginning of the covid-19 pandemic in 2020, but then rose markedly for the rest of the year, the US Centers for Disease Control and Prevention (CDC) has reported. Chlamydia declined slightly. The CDC cautioned that the data may be an undercount because of the pandemic.12345

In 2020 there were 2.4 million cases of sexually transmitted diseases (STDs), the CDC said. This included 677 769 cases of gonorrhoea (a 45% increase from 2016), 133 945 cases of syphilis (a 52% increase from 2016), 2145 cases of congenital syphilis (a 235% increase from 2016), and 1579 885 cases of chlamydia (a 1.2% decrease from 2016.)

Leandro Mena, director of CDC’s division of STD treatment, said the pandemic had increased awareness of what was long known about STDs, “Social and economic factors—such as poverty and health insurance status—create barriers, increase health risks, and often result in worse health outcomes for some people. If we are to make lasting progress we have to understand the systems that create inequities and work with partners to change them.”…
<https://www.bmj.com/content/377/bmj.o1275>

**international perspectives**

**title:** Covid-19: US hospitals continued to perform unnecessary surgeries during pandemic

BMJ |19th may 2022

US hospitals continued to perform eight overused and unnecessary surgical procedures for older patients during the first year of the pandemic, a study1 has shown.

Cardiologist Vikas Saini, president of the Lown Institute in Needham, Massachusetts, which carried out the research, said, “You couldn’t go into your local coffee shop during early days of the pandemic but hospitals brought people in for all kinds of unnecessary procedures. The fact that a pandemic barely slowed things down shows just how deeply entrenched overuse is in American healthcare.”

The non-profit institute studies ways to avoid unnecessary care. It was founded by the late Bernard Lown, co-winner of the 1985 Nobel peace prize, Harvard cardiologist, and developer of the direct current defibrillator and the cardioverter for correcting heart dysrhythmias.
<https://www.bmj.com/content/377/bmj.o1254>

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