COVID-19 Evidence Bulletin

15th November 2022

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| [Clinical Management](#Clinical) [Long-term Effects](#Long)  [Infection Control](#Infection) | [Public Health & Health Inequalities](#MentalHealth)  [Mental Health](#MentalHealth) | [Recovery](#Recovery)  [Health Management](#Management) |

**clinical management**

**title:** Evusheld protects the most vulnerable patients, analysis shows [news]

bmj| 8th november 2022

The antibody drug Evusheld is effective for protecting clinically extremely vulnerable people from covid-19, including its omicron variants, a preprint study has reported…The prophylactic treatment, manufactured by AstraZeneca, is a combination of two long acting antibodies (tixagevimab and cilgavimab). It is given as two separate, sequential intramuscular injections in the same session and can be administered in the community.

A research team, led by the University of Birmingham alongside academics from King’s College London and the UK Health Security Agency, carried out a systematic review and meta-analysis to examine its effectiveness in immunocompromised patients…

The study’s senior investigator, Lennard Lee, senior research fellow at the University of Birmingham and academic medical oncologist at the University of Oxford, said, “There is strong evidence emerging across the world that this approach of using prophylactic antibody therapies in combination with vaccination is a revolutionary approach to safeguard the most vulnerable patients this winter. The science and data suggest that it would be a successful approach for many cancer and immunocompromised patients at the highest level of risk.”…

For the meta-analysis, reviewers included six studies that compared a tixagevimab and cilgavimab intervention group with a control group. They all reported on the primary outcome of breakthrough SARS-CoV-2 infections after tixagevimab/cilgavimab administration, with covid related hospital admissions, intensive treatment admissions, and mortality assessed as secondary outcomes…

They concluded, “This systematic review has illustrated that there is now a growing body of real-world evidence validating the original phase 3 study as to the clinical effectiveness of tixagevimab/cilgavimab and demonstrating effectiveness in the omicron era. It is critically important that larger-scale and better-controlled pilots and evaluations are performed to highlight the significant clinical benefit of prophylactic antibody treatment in immunocompromised groups.”…

A spokesperson for the Department of Health and Social Care for England said that the government would not be procuring any doses “at this time.” They said that the UK National Institute of Health and Care Excellence had begun its appraisal of Evusheld and that should the treatment prove to be clinically and cost effective “it will be made available on the NHS in the usual way.”

<https://www.bmj.com/content/379/bmj.o2690>

**long-term effects**

**title:** Cognitive Deficits in Long Covid-19

nejm | 10th november 2022

Some patients who have recovered from an infection have reported transient or even lasting cognitive dysfunction. This includes patients who have been infected with SARS-CoV-2, many of whom, including those with mild disease, have reported deficits in attention, executive functioning, language, processing speed, and memory — symptoms collectively referred to as “brain fog.” Together with increased incidence of anxiety, depression, sleep disorder, and fatigue, this syndrome of cognitive impairment contributes substantially to the morbidity of post–Covid-19 conditions (also called “long Covid”).

Nevertheless, Covid-related brain fog is difficult to diagnose and to separate from other reasons for the symptoms in an individual patient, because neurocognitive longitudinal data for patients are rarely available. (On a population level, however, cognitive decline after Covid has been documented… Physicians are generally reluctant to accept a condition as an organic disease without a pathobiologic concept or the ability to measure the disease in a given patient, as is the case with post-Covid brain fog. Results of a study recently reported by Fernández-Castañeda and colleagues may represent a pivot in our understanding of this sequela…

Although the findings of brain dysfunction and patterns of damage during and after Covid are worrisome, especially given the similarities with changes in human neurodegenerative diseases,…translational studies such as the one reported by Fernández-Castañeda may point to paths toward accurate diagnoses and treatments.

<https://www.nejm.org/doi/full/10.1056/NEJMcibr2210069>

**infection control**

**title:** SARS-CoV-2 seroprevalence, cumulative infections, and immunity to symptomatic infection – A multistage national household survey and modelling study, Dominican Republic, June–October 2021

the lancet regional news - americas| 8th November 2022

Summary

Background

Population-level SARS-CoV-2 immunological protection is poorly understood but can guide vaccination and non-pharmaceutical intervention priorities. Our objective was to characterise cumulative infections and immunological protection in the Dominican Republic.

Methods

Household members ≥5 years were enrolled in a three-stage national household cluster serosurvey in the Dominican Republic. We measured pan-immunoglobulin antibodies against the SARS-CoV-2 spike (anti-S) and nucleocapsid glycoproteins, and pseudovirus neutralising activity against the ancestral and B.1.617.2 (Delta) strains. Seroprevalence and cumulative prior infections were weighted and adjusted for assay performance and seroreversion. Binary classification machine learning methods and pseudovirus neutralising correlates of protection were used to estimate 50% and 80% protection against symptomatic infection…

Interpretation

Cumulative infections substantially exceeded prior estimates and overall immunological exposure was high. After controlling for confounders, markedly lower immunological protection was observed to the ancestral and Delta strains across certain subgroups, findings that can guide public health interventions and may be generalisable to other settings and viral strains…

<https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(22)00207-1/fulltext>

**title:** Safety of BNT162b2 or CoronaVac COVID-19 vaccines in patients with heart failure: A self-controlled case series study

the lancet regional health – western pacific | 7th november 2022

Summary

Background

COVID-19 vaccines are important for patients with heart failure (HF) to prevent severe outcomes but the safety concerns could lead to vaccine hesitancy. This study aimed to investigate the safety of two COVID-19 vaccines, BNT162b2 and CoronaVac, in patients with HF.

Findings

We identified 32,490 patients with HF, of which 3035 were vaccinated and had a hospitalization for HF during the observation period (BNT162b2 = 755; CoronaVac = 2280). There were no increased risks during the 0–13 days (IRR 0.64 [95% confidence interval 0.33–1.26]; 0.94 [0.50–1.78]; 0.82 [0.17–3.98]) and 14–27 days (0.73 [0.35–1.52]; 0.95 [0.49–1.84]; 0.60 [0.06–5.76]) after the first, second and third doses of BNT162b2. No increased risks were observed for CoronaVac during the 0–13 days (IRR 0.60 [0.41–0.88]; 0.71 [0.45–1.12]; 1.64 [0.40–6.77]) and 14–27 days (0.91 [0.63–1.32]; 0.79 [0.46–1.35]; 1.71 [0.44–6.62]) after the first, second and third doses. We also found no increased risk of MACE or all hospitalization after vaccination.

Interpretation

Our results showed no increased risk of hospitalization for HF, MACE or all hospitalization after receiving BNT162b2 or CoronaVac vaccines in patients with HF...

<https://www.thelancet.com/journals/lanwpc/article/PIIS2666-6065(22)00245-0/fulltext>

**title:** Six-Month Follow-up after a Fourth BNT162b2 Vaccine Dose [letters]

NEJM| 9th november 2022

In a prospective cohort study involving health care workers that was described previously,… we evaluated the humoral response and vaccine effectiveness of a fourth dose of the BNT162b2 vaccine (Pfizer–BioNTech) against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during a 6-month follow-up period in which omicron (mostly BA.1 and BA.2) was the predominant variant in Israel…

In this prospective cohort study, a third dose of the BNT162b2 vaccine led to an improved and sustained immunologic response as compared with two doses, but the additional immunologic advantage of the fourth dose was much smaller and had waned completely by 13 weeks after vaccination. This finding correlated with waning vaccine effectiveness among recipients of a fourth dose, which culminated in no substantial additional effectiveness over a third dose at 15 to 26 weeks after vaccination. These results suggest that the fourth dose, and possibly future boosters, should be timed wisely to coincide with disease waves or to be available seasonally, similar to the influenza vaccine. Whether multivalent booster doses will result in longer durability remains to be seen.

<https://www.nejm.org/doi/full/10.1056/NEJMc2211283?query=featured_coronavirus>

**title:** Lifting Universal Masking in Schools — Covid-19 Incidence among Students and Staff

NEJM | 9th november 2022  
  
Abstract

Background

In February 2022, Massachusetts rescinded a statewide universal masking policy in public schools, and many Massachusetts school districts lifted masking requirements during the subsequent weeks. In the greater Boston area, only two school districts — the Boston and neighboring Chelsea districts — sustained masking requirements through June 2022. The staggered lifting of masking requirements provided an opportunity to examine the effect of universal masking policies on the incidence of coronavirus disease 2019 (Covid-19) in schools.

Methods

We used a difference-in-differences analysis for staggered policy implementation to compare the incidence of Covid-19 among students and staff in school districts in the greater Boston area that lifted masking requirements with the incidence in districts that sustained masking requirements during the 2021–2022 school year. Characteristics of the school districts were also compared.

Results

Before the statewide masking policy was rescinded, trends in the incidence of Covid-19 were similar across school districts. During the 15 weeks after the statewide masking policy was rescinded, the lifting of masking requirements was associated with an additional 44.9 cases per 1000 students and staff (95% confidence interval, 32.6 to 57.1), which corresponded to an estimated 11,901 cases and to 29.4% of the cases in all districts during that time. Districts that chose to sustain masking requirements longer tended to have school buildings that were older and in worse condition and to have more students per classroom than districts that chose to lift masking requirements earlier. In addition, these districts had higher percentages of low-income students, students with disabilities, and students who were English-language learners, as well as higher percentages of Black and Latinx students and staff. Our results support universal masking as an important strategy for reducing Covid-19 incidence in schools and loss of in-person school days. As such, we believe that universal masking may be especially useful for mitigating effects of structural racism in schools, including potential deepening of educational inequities.

Conclusions

Among school districts in the greater Boston area, the lifting of masking requirements was associated with an additional 44.9 Covid-19 cases per 1000 students and staff during the 15 weeks after the statewide masking policy was rescinded.

<https://www.nejm.org/doi/full/10.1056/NEJMoa2211029>

**public health & health inequalities**

**title:** Vaccine access: World’s poorest people suffer at the hands of free market dynamics, says WHO [news]

bmj| 10th november 2022

Important progress on vaccine access has been made over the past two decades, but diseases associated with markets that are deemed to have little commercial value “remain neglected,” the World Health Organization has warned…

In its Global Vaccine Market Report 2022 WHO says that inequitable distribution is not an issue unique to covid-19 vaccines, as poorer countries have been “consistently struggling” to get vaccines that wealthier countries also want.

It says that the vaccine equity problems faced during the covid-19 pandemic have shone a light on the issues experienced in other vaccine markets, such as the human papillomavirus (HPV) vaccine against cervical cancer, which has been introduced in only 41% of low income countries but 83% of high income countries….

WHO’s director general, Tedros Adhanom Ghebreyesus, said, “The right to health includes the right to vaccines, and yet this new report shows that free market dynamics are depriving some of the world’s poorest and most vulnerable people of that right. WHO is calling for much needed changes to the global vaccine market to save lives, prevent disease, and prepare for future crises.”…

<https://www.bmj.com/content/379/bmj.o2714>

**title:** Covid-19: England’s health declined in 2020, but not across all areas [news]

BMJ | 9th november 2022

The health of the population in England declined in 2020 during the early stages of the pandemic, although there was a mixed picture across different areas of health, official data from the Office for National Statistics (ONS) show…

The Health Index for England declined from 100.5 in 2019 to 100.1 in 2020, driven largely by falls on indicators relating to personal wellbeing and mortality. But the data also show improvements in some areas that were likely to have been affected by pandemic preventative measures.

Emma Rourke, interim deputy national statistician (health, population, and methods) at the ONS, explained, “We can see that there was an improvement in the Healthy Places domain in part because of factors such as better air quality, fewer road accidents, and less crime impact. This was likely driven by the need for people to stay at home at this time. However, the score for the Healthy People category declined considerably, which reflects the impact the pandemic had on mental health and wellbeing.”…

<https://www.bmj.com/content/379/bmj.o2710>

**title:** Tuberculosis control: getting back on track in the era of COVID-19

the lancet respiratory medicine | 9th november 2022

A new report by WHO has laid bare the worrying extent to which the COVID-19 pandemic has disrupted efforts to combat tuberculosis. At the centre of the 2022 Global Tuberculosis Report are the statistics on case notifications. In 2019, the year before the COVID-19 pandemic was declared, 7·1 million new cases of tuberculosis were reported worldwide. In 2020, this number dropped to 5·8 million, before recovering somewhat to 6·4 million in 2021. WHO is confident that the reduced number of reported cases of tuberculosis does not represent a genuine drop in the disease burden. The most likely explanation is, instead, that the first 2 years of the pandemic saw dramatically reduced access to health care and diagnostic services…

The WHO report also notes that the COVID-19 pandemic is likely to have stalled or reversed progress in achieving not only global tuberculosis targets, but also universal health coverage, which will in turn affect prevention and control of tuberculosis. The ongoing armed conflicts, energy crisis, and rampant inflation that have beset countries across the world will compound the problem. “Undernutrition is one of the key drivers of tuberculosis”, said Kasaeva. “We are seeing rising poverty and food insecurity, and that will certainly have an impact on tuberculosis.”

Much depends on the speed at which high-burden countries are able to get back on track. “We need to see urgent efforts and rapid success in catching up on diagnosing people with tuberculosis to mitigate the effects of the pandemic”, said Katherine Floyd, who led the team that produced the Global Tuberculosis Report 2022. “Unless that happens, we will be continually adding to the number of undiagnosed people in the community, leaving them at high risk of dying from tuberculosis and infecting others.”

<https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00442-8/fulltext>

**mental health**

**title:** Case 34-2022: A 57-Year-Old Woman with Covid-19 and Delusions

nejm | 10th november 2022   
  
A 57-year-old woman with major depressive disorder and coronavirus disease…was evaluated at a hospital…because she was having delusions that she was dead.

The patient had been in her usual state of health until 2 weeks before this presentation, when myalgias, cough, sore throat, nausea, and vomiting developed. She sought evaluation at the primary care clinic of an academic medical center…Nucleic acid testing of a nasopharyngeal swab was positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA, and the patient was instructed to quarantine at home. She lived with her father and assisted him with activities of daily living; he also received a diagnosis of Covid-19…

Could this patient’s neuropsychiatric symptoms be related to her recent diagnosis of Covid-19? Early studies suggested that more than one third of patients with Covid-19 had a neuropsychiatric syndrome…

Some cases of Covid-19 lead to persistent symptoms or long-term complications that extend beyond acute disease (a condition sometimes referred to as postacute syndrome of Covid-19 or “long Covid”)… In such cases, neuropsychiatric symptoms can include fatigue, myalgias, headache, anxiety, depression, dysautonomia, and cognitive impairment (also referred to as “brain fog”)…

Final Diagnosis

Cotard’s syndrome, catatonia, depression, and seizure after coronavirus disease…

<https://www.nejm.org/doi/full/10.1056/NEJMcpc2115857?query=featured_coronavirusontent/379/bmj.o2122>

**recovery**

**title:** How similar is covid-19 to the flu? [feature]

bmj| 10th November 2022

Chris Stokel-Walker asks whether what we’ve learnt about covid-19 makes the comparison to influenza fair and correct…

As the pandemic progressed, groups of experts…began talking about the possible evolution of SARS-CoV-2 into something more “flu-like”—the natural extension, as some virologists thought, of a virus getting less deadly so that it could continue to propagate in the population. By killing fewer hosts, there is a higher chance that the virus will be transmitted to others. Emma Thomson, professor in infectious diseases at the MRC-University of Glasgow Centre for Virus Research, told The BMJ in a video, “I learnt at medical school that viruses generally get less severe. But I think that’s probably one of those statements that’s made with very little evidence behind it. We’ve never watched evolution like [SARS-CoV-2] on such a large scale and with so much sequencing of the [viral genome being done]. So we now have much better evidence to show that there’s a real heterogeneity [in the way that viruses evolve].” …

Finally, there’s the disease covid-19 itself and the way that we are coming to “live with the virus” in the same way that each year we live with influenza, which kills 290 000 to 650 000 people globally each year, according to the World Health Organization.

What do the viruses target?

Both SARS-CoV-2 and the influenza virus target the respiratory epithelium…

There are differences…Influenza requires haemagglutinin and neuraminidase, whereas SARS-CoV-2 uses protein S to infect humans…

How do their symptoms differ?

There are similarities…a sore throat, a runny nose, and perhaps a general sense of fever and achiness. But,…covid-19 has caused a range of symptoms not usually seen with the flu…people lose their sense of smell and taste…

One difference between the two is that SARS-CoV-2 seems to sometimes trigger a more substantial immune response, which makes some people very ill…

How does mortality compare?

In the early days of the pandemic, covid-19’s infection fatality ratio (IFR)—the proportion of people who died after contracting the disease—was much higher than the flu’s…

One non-academic analysis indicated that covid-19’s IFR has now become equal to or less than flu’s (around 0.04%), whereas in mid-2020 covid-19 was 20 times more likely to kill people than the flu…

What about variants?

…SARS-CoV-2 mutates and evolves, forming new variants that have been fuelling fresh waves. This pattern of behaviour is similar to what happens each year with new variants of influenza…

A big difference with SARS-CoV-2 is that it has evolved much faster…Unlike influenza, this has continued even through warmer months, posing a challenge for vaccination efforts to keep up.

How is vaccination handled?

The pandemic is now centred around new variants and waning immunity, with an emphasis on regular booster jabs, particularly tweaked to the new variants, to top up immunity…This is not dissimilar to the yearly flu jab, although the speed at which new covid variants are emerging is a problem for the development of new booster vaccine formulations…

The increasing similarity with the flu jab campaign is likely to continue…

What about treatments?

Besides vaccines, we now have a range of treatments for covid-19, including antivirals…

…it’s difficult to compare the rapid rise and use of covid-19 interventions with flu treatments that are rarely used.

Steroids like dexamethasone, for example, are now a core first line therapy for covid-19. But if a patient comes into hospital with severe flu, we don’t give them steroids in the UK…

This is a missed opportunity, says Barclay. “There are lots of things we can learn about what to do with flu from SARS, and what some people have been thinking about is using these small molecules more like prophylactics, getting them into people very quickly,” she says; for example, monoclonal antibodies could be used to treat flu just as we have with covid-19.

Are there similarities in the ways the two diseases are perceived?

Before the pandemic, England and Wales, along with other countries, would “accept” between 10 000 and 25 000 deaths a year caused by influenza… And it’s arguable that countries opening up and living largely as if the pandemic is not ongoing signals a similar acceptance of the still high numbers of deaths from covid-19—–as of 23 September 2022, 44 341 deaths in England and Wales in 2022 were marked as caused by or involving covid-19…

“I think we will continue to try and strike the balance between the numbers, and how uncomfortable those numbers feel, and how uncomfortable the hospital situation is. Basically, everything will be predicated on whether the NHS can cope…

…encounters with covid are becoming common, with some degree of immunity from exposure to prior variants, vaccination, or both helping to lessen their severity—so far…

<https://www.bmj.com/content/379/bmj.o2625>

**title:** Living with COVID-19 and preparing for future pandemics: revisiting lessons from the HIV pandemic

the lancet HIV | 9th november 2022

Summary

In April, 2020, just months into the COVID-19 pandemic, an international group of public health researchers published three lessons learned from the HIV pandemic for the response to COVID-19, which were to: anticipate health inequalities, create an enabling environment to support behavioural change, and engage a multidisciplinary effort. We revisit these lessons in light of more than 2 years’ experience with the COVID-19 pandemic. With specific examples, we detail how inequalities have played out within and between countries, highlight factors that support or impede the creation of enabling environments, and note ongoing issues with the scarcity of integrated science and health system approaches. We argue that to better apply lessons learned as the COVID-19 pandemic matures and other infectious disease outbreaks emerge, it will be imperative to create dialogue among polarised perspectives, identify shared priorities, and draw on multidisciplinary evidence…

<https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00301-0/fulltext>

**health management**

**title:** Covid-19 vaccination in the UK: the Joint Committee on Vaccination and Immunisation’s infrastructure [Letters]

bmj| 9th november 2022

Healthcare professionals know the importance of seeking help during emergencies. For example, the Resuscitation Council UK states in its adult basic life support guidelines that on recognition of a cardiac arrest the next step is to “shout for nearby help and dial 999.”…

I write to ask what might seem a prosaic question. Did the Joint Committee on Vaccination and Immunisation (JCVI) shout early for additional administrative help during the pandemic? If it did, was anyone listening?...

<https://www.bmj.com/content/379/bmj.o2685>

We

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