COVID-19 weekly update

23rd April 2021

**clinical management**

**Title:** Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia

New England Journal of Medicine | 22nd April 2021

Coronavirus disease 2019 is associated with immune dysregulation and hyperinflammation, including elevated interleukin-6 levels. The use of tocilizumab, a monoclonal antibody against the interleukin-6 receptor, has resulted in better outcomes in patients with severe Covid-19 pneumonia in case reports and retrospective observational cohort studies. Data are needed from randomized, placebo-controlled trials.

In this phase 3 trial, the authors randomly assigned 452 patients who were hospitalized with severe Covid-19 pneumonia in a 2:1 ratio receive a single intravenous infusion of tocilizumab (at a dose of 8 mg per kilogram of body weight) or placebo. Approximately one quarter of the participants received a second dose of tocilizumab or placebo 8 to 24 hours after the first dose. The primary outcome was clinical status at day 28 on an ordinal scale ranging from 1 (discharged or ready for discharge) to 7 (death) in the modified intention-to-treat population, which included all the patients who had received at least one dose of tocilizumab or placebo.

In this randomized trial involving hospitalized patients with severe Covid-19 pneumonia, the use of tocilizumab did not result in significantly better clinical status or lower mortality than placebo at 28 days.

Full article: [Tocilizumab in hospitalized patients with severe Covid-19 pneumonia](https://www.nejm.org/doi/pdf/10.1056/NEJMoa2028700?articleTools=true)

**Title:** Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19

New England Journal of Medicine | 22nd April 2021

The efficacy of interleukin-6 receptor antagonists in critically ill patients with coronavirus disease 2019 (Covid-19) is unclear. The authors of this study evaluated tocilizumab and sarilumab in an ongoing international, multifactorial, adaptive platform trial.

Adult patients with Covid-19, within 24 hours after starting organ support in the intensive care unit (ICU), were randomly assigned to receive tocilizumab (8 mg per kilogram of body weight), sarilumab (400 mg), or standard care (control). The primary outcome was respiratory and cardiovascular organ support–free days, on an ordinal scale combining in-hospital death (assigned a value of −1) and days free of organ support to day 21. The trial uses a Bayesian statistical model with predefined criteria for superiority, efficacy, equivalence, or futility. An odds ratio greater than 1 represented improved survival, more organ support–free days, or both.

In critically ill patients with Covid-19 receiving organ support in ICUs, treatment with the interleukin-6 receptor antagonists tocilizumab and sarilumab improved outcomes, including survival.

Full article: [Interleukin-6 Receptor Antagonists in critically ill patients with Covid-19](https://www.nejm.org/doi/pdf/10.1056/NEJMoa2100433?articleTools=true)

See also: [For adults with COVID‐19, what are the effects of the interleukin‐6 blocking agents tocilizumab and sarilumab?](https://www.cochranelibrary.com/cca/doi/10.1002/cca.3607/full?cookiesEnabled) | Cochrane Clinical Answers

**Title:** Compassionate Use of Remdesivir in Children With Severe COVID-19

Pediatrics | April 2021

Remdesivir shortens time to recovery in adults with severe coronavirus disease 2019 (COVID-19), but its efficacy and safety in children are unknown. This paper describes outcomes in children with severe COVID-19 treated with remdesivir.

Seventy-seven hospitalized patients <18 years old with confirmed severe acute respiratory syndrome coronavirus 2 infection received remdesivir through a compassionate-use program between March 21 and April 22, 2020. The intended remdesivir treatment course was 10 days (200 mg on day 1 and 100 mg daily subsequently for children ≥40 kg and 5 mg/kg on day 1 and 2.5 mg/kg daily subsequently for children <40 kg, given intravenously). Clinical data through 28 days of follow-up were collected.

Among 77 children treated with remdesivir for severe COVID-19, most recovered and the rate of serious adverse events was low. Remdesivir was well tolerated, with a low incidence of serious adverse events (16%). Most adverse events were related to COVID-19 or comorbid conditions. Laboratory abnormalities, including elevations in transaminase levels, were common; 61% were grades 1 or 2.

Full abstract: [Compassionate use of Remdesivir in children with severe COVID-19](https://pediatrics.aappublications.org/content/early/2021/04/19/peds.2020-047803?ijkey=3cee193ec5a0b7bc8e31f6025f62081be5626ab7&keytype2=tf_ipsecsha)

**Title:** Previous infections could shorten COVID illness

medRxiv | 19th April 2021

Recent infection by viruses related to SARS-CoV-2 could reduce the duration of COVID-19, according to an analysis of antibodies from 2,000 health-care workers.

Antibodies against the SARS-CoV-2 spike protein can be powerful defences against COVID-19. But some people have rare antibodies against other coronaviruses that pre-date the pandemic and can bind to SARS-CoV-2 proteins other than spike. To search for a possible link between such antibodies and protection from COVID-19, researchers studied antibody levels and infection status in about 2,000 local volunteers during two COVID-19 surges. The team found that people with the rare, pre-pandemic antibodies that work against SARS-CoV-2 were not protected from contracting the virus and developing COVID-19. But high concentrations of other antibodies that had been elicited by two betacoronaviruses — a category that includes SARS-CoV-2 — were associated with a quicker recovery from COVID-19 symptoms.

The authors speculate that this protection is provided by immune-system players called T cells that were generated in response to previous betacoronavirus infection.

Full paper: [Sero-monitoring of health care workers reveals complex relationships between common coronavirus antibodies and SARS-CoV-2 severity](https://www.medrxiv.org/content/10.1101/2021.04.12.21255324v1.full.pdf)

**recovery**

**Title:** Government launches COVID-19 Antivirals Taskforce to roll out innovative home treatments this autumn

Department of Health & Social Care | 20th April 2021

A new Antivirals Taskforce has been launched by the government to identify treatments for UK patients who have been exposed to COVID-19 to stop the infection spreading and speed up recovery time.

The taskforce will search for the most promising novel antiviral medicines that can be taken at home and support their development through clinical trials to ensure they can be rapidly rolled out to patients as early as the autumn. The taskforce will also look at opportunities to onshore the manufacture of antiviral treatments.

The aim is to have at least 2 effective treatments this year, either in a tablet or capsule form, that the public can take at home following a positive COVID-19 test or exposure to someone with the virus.

Full detail: [Government launches COVID-19 Antivirals Taskforce to roll out innovative home treatments this autumn](https://www.gov.uk/government/news/government-launches-covid-19-antivirals-taskforce-to-roll-out-innovative-home-treatments-this-autumn)

**Title:** Favipiravir to be investigated as a possible COVID-19 treatment for at-home recovery in the PRINCIPLE trial

National Institute for Health Research | 8th April 2021

The antiviral drug favipiravir will be studied as a treatment for COVID-19 in people recovering at home and in community settings, in a clinical trial funded and supported by the NIHR. Favipiravir becomes the sixth treatment to be studied in the PRINCIPLE trial-The Platform Randomised trial of Interventions against COVID-19 In older peoPLE- is the largest trial occurring in community settings.

Favipiravir is an antiviral drug that has been licenced in Japan since 2014 to treat influenza. It works by inhibiting a viral enzyme called RNA polymerase, preventing viral replication within human cells. This viral enzyme is common to several viruses, including SARS-CoV-2, which causes COVID-19. The drug has shown positive results against SARS-CoV-2 in laboratory and animal studies, with small pilot studies in humans demonstrating some benefit in reducing symptoms and the duration of illness.

Now, experts will study the potential treatment after University of Oxford researchers and trial steering committee leading the trial in conjunction with the Chief Medical Officer, following a recommendation by the UK COVID-19 Therapeutics Advisory Panel.

Full press release: [Favipiravir to be investigated as a possible COVID-19 treatment for at-home recovery in the PRINCIPLE trial](https://www.nihr.ac.uk/news/favipiravir-to-be-investigated-as-a-possible-covid-19-treatment-for-at-home-recovery-in-the-principle-trial/27426)

**Title:** A Multidisciplinary NHS COVID-19 Service to Manage Post-COVID-19 Syndrome in the Community

Journal of Primary Care & Community Health| 21st April 2021

This paper is authored by staff from Leeds Community Healthcare NHS Trust and Leeds Teaching Hospitals NHS Trust, Leeds. They explain how the Community COVID-19 MDT pathway was established in September 2020, as part of the NHS England “Five-point plan” to embed post-COVID-19 syndrome assessment clinics across England. A service evaluation was conducted to capture the proportion of patients still suffering from persistent symptoms 7 weeks after hospital discharge. This led to ring-fenced funding for a COVID rehabilitation service and the establishment of a 3 tier model of post COVID management.

The authors describe the configuration of a functioning comprehensive multidisciplinary rehabilitation pathway for those in Leeds experiencing long term impacts after COVID-19 to help inform the development of these services in the UK and worldwide. Their intention for this article is to provide insight into the development of a dedicated COVID-19 Community MDT, and a template for establishing a pathway of care.

Full article: [A multidisciplinary NHS COVID-19 service to manage post-covid-19 syndrome in the community](https://journals.sagepub.com/doi/pdf/10.1177/21501327211010994)

**Title:** Primary care networks and place-based working: addressing health inequalities in a Covid-19 world

The Health Creation Alliance | 20th April 2021

COVID-19 has accelerated the formation of and action being taken by local networks in the community, giving communities and local partners an urgency, a higher priority and a confidence to act to support members of the community in many ways. The vaccination programme has accelerated the coming together of practices within Primary Care Networks (PCNs) to create a whole new service. COVID-19 has also exposed the extent of health inequalities. What happens now is critical. Primary care, increasingly led by (PCNs), has a huge opportunity to work in more networked ways with communities and local partners to address health inequalities.

This report provides insights from those working to address health inequalities outside the NHS about how primary care, enabled by primary care networks, might access the breadth of potential solutions that are possible when they work in partnership with their communities and local partners.

Full report: [Primary care networks and place-based working: addressing health inequalities in a Covid-19 world](https://thehealthcreationalliance.org/wp-content/uploads/2021/04/PCNs-and-place-based-working-_addressing-health-inequalities-in-a-COVID-19-world_FINAL_1-April-2021.pdf)

**Title:** Learning from the community response to Covid-19: how the NHS can support communities to keep people well

The Health Creation Alliance | 20th April 2021

COVID-19 has affected communities in different ways and, for some, the effects of the pandemic have been devastating. It has also shone a harsh light on the underlying inequalities in society and reinforced the urgent need for society to do more to address health inequalities.

COVID-19 also demanded that the NHS adopts different ways of working. Examples include primary care focussing on digital methods to continue service delivery and acute trusts and systems having to prioritise and reorganise care processes and pathways. The NHS has learnt from this.

The NHS could also learn from how communities selforganised in response to COVID-19. If the different parts of the NHS respond, respect and connect well to networked and organised communities, this could support a better future in which inequalities are more effectively addressed.

This report considers what all community-facing NHS organisations can learn from the community response to Covid-19. The report outlines practical guidance and recommendations to help build a future where people are at the heart of keeping communities well.

Full report: [Learning from the community response to Covid-19: how the NHS can support communities to keep people well](https://thehealthcreationalliance.org/wp-content/uploads/2021/04/THCA-Report_Community-response-to-COVID-19_NHS-learning-FINAL_-April-2021.pdf)

**Title:** Covid 19: supporting the vulnerable during lockdown

House of Commons Public Accounts Committee| 21st April 2021

This report recognises the pace and urgency with which Government delivered the shielding programme. However, the report concludes that the programme suffered from the problems of poor data and a lack of joined up systems meaning that it took too long to identify some clinically vulnerable people at a time when their need was urgent.

The Committee says “clearly government has learned lessons which have fed into more recent iterations of shielding”, including much greater understanding of the range of covid19 risk factors, where DHSC’s initial, purely clinical approach to vulnerability omitted key characteristics such as ethnicity, postcode and Body Mass Index.

* Full report: [Covid 19: supporting the vulnerable during lockdown](https://publications.parliament.uk/pa/cm5801/cmselect/cmpubacc/938/93802.htm)
* Report summary: [Covid 19: supporting the vulnerable during lockdown](https://publications.parliament.uk/pa/cm5801/cmselect/cmpubacc/938/93803.htm)
* [Report conclusions and reccomendations](https://publications.parliament.uk/pa/cm5801/cmselect/cmpubacc/938/93805.htm)

Press release: [Central-command system failed to reach around 800k clinically extremely vulnerable people before hundreds of thousands added to local lists](https://committees.parliament.uk/committee/127/public-accounts-committee/news/154620/centralcommand-system-failed-to-reach-around-800k-clinically-extremely-vulnerable-people-before-hundreds-of-thousands-added-to-local-lists/)

See also: [Government’s shielding scheme failed thousands of clinically extremely vulnerable people, say MPs](https://www.bmj.com/content/373/bmj.n1033) | BMJ

**Title:** Spending on health in Europe: entering a new era

World Health Organisation | 22ndApril 2021

COVID-19 has shown the importance of robust health systems and the long-term benefits of investing in the health of the population. Countries were quick to mobilize additional funds for the health system in response to the pandemic, but treating and preventing COVID-19 and addressing the impact of disruption to services will require continued investment in the years ahead.

This report highlights the need for governments to maintain a higher level of public spending on health for the wider benefit of society despite expected budgetary pressures following the pandemic. The report states that sustained increases in public spending on health coupled with well designed public policy can mitigate the negative effects of COVID-19 while also building health system resilience.

The report also highlights that spending on primary health care accounts for less than half of all health spending, despite being a cost-effective way to deliver health care to communities. WHO has called for an additional 1% of gross domestic product (GDP) in public funding to be spent on primary health care.

Full report: [Spending on health in Europe: entering a new era](https://apps.who.int/iris/bitstream/handle/10665/340910/9789289055079-eng.pdf)

Press release: [New report from WHO on health spending calls on governments not to repeat past mistakes when rebuilding from COVID-19](https://www.euro.who.int/en/health-topics/Health-systems/health-systems-financing/news/news/2021/4/new-report-from-who-on-health-spending-calls-on-governments-not-to-repeat-past-mistakes-when-rebuilding-from-covid-19)

**Title:** High-dimensional characterization of post-acute sequalae of COVID-19

Nature | 22nd April 2021

As the COVID-19 pandemic has progressed, it has become clear that many survivors -- even those who had mild cases -- continue to manage a variety of health problems long after the initial infection should have resolved. In what is believed to be the largest comprehensive study of long COVID-19 to date, researchers showed that COVID-19 survivors -- including those not sick enough to be hospitalized -- have an increased risk of death in the six months following diagnosis with the virus.

The researchers also have catalogued the numerous diseases associated with COVID-19, providing a big-picture overview of the long-term complications of COVID-19 and revealing the massive burden this disease is likely to place on the world's population in the coming years.

The authors showed that, after surviving the initial infection (beyond the first 30 days of illness), COVID-19 survivors had an almost 60% increased risk of death over the following six months compared with the general population. At the six-month mark, excess deaths among all COVID-19 survivors were estimated at eight people per 1,000 patients. Among patients who were ill enough to be hospitalized with COVID-19 and who survived beyond the first 30 days of illness, there were 29 excess deaths per 1,000 patients over the following six months.

The researchers confirmed that, despite being initially a respiratory virus, long COVID-19 can affect nearly every organ system in the body. The researchers identified newly diagnosed major health issues that persisted in COVID-19 patients over at least six months and that affected nearly every organ and regulatory system in the body, including:

* Respiratory system: persistent cough, shortness of breath and low oxygen levels in the blood.
* Nervous system: stroke, headaches, memory problems and problems with senses of taste and smell.
* Mental health: anxiety, depression, sleep problems and substance abuse.
* Metabolism: new onset of diabetes, obesity and high cholesterol.
* Cardiovascular system: acute coronary disease, heart failure, heart palpitations and irregular heart rhythms.
* Gastrointestinal system: constipation, diarrhea and acid reflux.
* Kidney: acute kidney injury and chronic kidney disease that can, in severe cases, require dialysis.
* Coagulation regulation: blood clots in the legs and lungs.
* Skin: rash and hair loss.
* Musculoskeletal system: joint pain and muscle weakness.
* General health: malaise, fatigue and anemia.

Full article: [High-dimensional characterization of post-acute sequalae of COVID-19](https://www.nature.com/articles/s41586-021-03553-9_reference.pdf)

**Title:** The Manchester Briefing COVID-19: International lessons for local and national government recovery and renewal

Alliance MBS | 23rd April 2021

The Manchester Briefing on COVID-19 is aimed at those who plan and implement recovery from COVID-19, including government emergency planners and resilience officers. The briefing brings together international lessons and examples which may prompt your thinking on the recovery from COVID-19, as well as other information from a range of sources.

This latest briefing shares lessons from:

* India – rethinking ‘vulnerability’ post-COVID
* Italy – places of remembrance following the pandemic
* USA – supporting ethnic minority-owned businesses
* Ireland – rural development priorities for recovery and renewal
* RCN – climate-ready infrastructure
* Sri Lanka – risk communications
* Dominica – community participation for resilience-building
* UK – social renewal from COVID-19

Full detail: [The Manchester Briefing on COVID-19](https://www.communigator.co.uk/login/Instances/uomhumscommslz/Documents/themanchesterbriefingoncovid-19b34-23rdapril.pdf?gator_td=l%2fXwvyBn5xYKF3tQYt3DNR07LwYon9IQjpyfGf%2fcbiER6CTdwG7Ojun2CWDTfFwOS9nHfWWJ6VEiyY9QBwwkLrRM4mNIpHom8z3VxEjkb%2b0qLsJOaxMtmLxg7Oyp1ecP5yY8oYYBg1HI%2bwrc6gTzgg%3d%3d)

Alliance MBS have also this week launched a new website: [Recovery, Renewal, Resilience](https://www.alliancembs.manchester.ac.uk/research/recovery-renewal-resilience-from-covid-19/?gator_td=l%2fXwvyBn5xYKF3tQYt3DNR07LwYon9IQjpyfGf%2fcbiER6CTdwG7Ojun2CWDTfFwOS9nHfWWJ6VEiyY9QBwwkLrRM4mNIpHom8z3VxEjkb%2b0qLsJOaxMtmLxg7Oyp1ecP5yY8oYYBg1HI%2bwrc6gTzgg%3d%3d)

**Infection control**

**Title:** JCVI issues new advice on COVID-19 vaccination for pregnant women

Public Health England | 16th April 2021

There have been no specific safety concerns identified with any brand of coronavirus (COVID-19) vaccines in relation to pregnancy.

Real-world data from the United States shows that around 90,000 pregnant women have been vaccinated, mainly with mRNA vaccines including Pfizer-BioNTech and Moderna, without any safety concerns being raised.

Based on this data, the Joint Committee on Vaccination and Immunisation (JCVI) advises that it’s preferable for pregnant women in the UK to be offered the Pfizer-BioNTech or Moderna vaccines where available. There is no evidence to suggest that other vaccines are unsafe for pregnant women, but more research is needed.

Full detail: [JCVI issues new advice on COVID-19 vaccination for pregnant women](https://www.gov.uk/government/news/jcvi-issues-new-advice-on-covid-19-vaccination-for-pregnant-women)

See also: [Pregnant women should be offered Pfizer or Moderna vaccine, says UK advisory committee](https://www.bmj.com/content/373/bmj.n1013) | BMJ

**Title:** Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

New England Journal of Medicine | 21st April 2021

Many pregnant persons in the United States are receiving messenger RNA (mRNA) coronavirus disease 2019 (Covid-19) vaccines, but data are limited on their safety in pregnancy.

This article reports that preliminary data from the CDC “v-safe after vaccination health checker” surveillance system, the v-safe pregnancy registry, and the Vaccine Adverse Event Reporting System did not show any obvious safety signals among pregnant persons who received mRNA Covid-19 vaccines.

The authors state that more data are needed to better inform maternal, pregnancy, and infant outcomes.

Full article: [Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons](https://www.nejm.org/doi/pdf/10.1056/NEJMoa2104983?articleTools=true)

**Title:** Will the Large-scale Vaccination Succeed in Containing the COVID-19 Epidemic and How Soon?

medRxiv | 18th April 2021

*This article is a preprint and has not been certified by peer review. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.*

The availability of vaccines provides a promising solution to containing the COVID-19 pandemic. This paper develops an epidemiological model to quantitatively analyze and predict the epidemic dynamics of COVID-19 under vaccination. The model is applied to the daily released numbers of confirmed cases of Israel and United States of America to explore and predict the trend under vaccination based on their current epidemic status and intervention measures.

For Israel, of which 53.83% of the population was fully vaccinated, under the current intensity of NPIs and vaccination scheme, the pandemic is predicted to end between May 14, 2021 to May 16, 2021 depending on an immunity duration between 180 days and 365 days; Assuming no NPIs after March 24, 2021, the pandemic will ends later, between July 4, 2021 to August 26, 2021. For USA, if we assume the current vaccination rate (0.268% per day) and intensity of NPIs, the pandemic will end between February 3, 2022 and August 17, 2029 depending on an immunity duration between 180 days and 365 days. However, assuming an immunity duration of 180 days and with no NPIs, the pandemic will not end, and instead reach an equilibrium state with a proportion of the population remaining actively infected.

Overall the daily vaccination rate should be chosen according to the vaccine efficacy and the immunity duration to achieve herd immunity. In some situations, vaccination alone cannot stop the pandemic, and NPIs are necessary both to supplement vaccination and accelerate the end of the pandemic. Considering that vaccine efficacy and duration of immunity may be reduced for new mutant strains, it is necessary to remain cautiously optimistic about the prospect of the pandemic under vaccination.

Full paper: [Will the large-scale vaccination succeed in containing the Covid-19 epidemic and how soon?](https://www.medrxiv.org/content/10.1101/2021.04.16.21255543v1.full.pdf)

**Title:** Lateral flow tests in care homes failed to stop outbreaks, finds study

BMJ | 2021; 373: n1025 | 20th April 2021

Lateral flow tests did not reduce the number or scale of covid-19 outbreaks in England’s care homes and caused excessive workload for staff, concludes research on the effects of testing staff and visitors.

The preprint, made available through the Social Science Research Network, compared outbreaks in care homes that piloted the rapid tests in Liverpool with those in homes in the same area that weren’t in the pilot. The research, commissioned by the Department of Health and Social Care, and which has not yet been peer reviewed, found that six of the 11 pilot homes had outbreaks of covid-19 and that only one had a positive result from lateral flow testing before the outbreak.

Staff were tested twice a week with self administered Innova rapid tests, while visitors were required to provide the care home with two negative rapid test results, taken within 24 hours, before they visited. The research team, which included one researcher who works with AstraZeneca, interviewed staff and found that testing protocol adherence was poor, with just 8.6% of staff achieving more than 75% adherence to protocol and 25.3% achieving more than or equal to 50%.

Further detail: [Lateral flow tests in care homes failed to stop outbreaks, finds study](https://www.bmj.com/content/373/bmj.n1025)

Full research paper: [Enhanced Lateral Flow Testing Strategies in Care Homes Are Associated with Poor Adherence and Were Insufficient to Prevent COVID-19 Outbreaks. Results from a Mixed Methods Implementation Study](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3822257)

**Title:** 9 in 10 pharmacies now offering free, rapid coronavirus (COVID-19) tests

Department of Health & Social Care | 19th April 2021

Nine in ten pharmacies across England are now distributing free rapid lateral flow tests for people to collect and use at home. Rapid, regular testing is now available to everyone in England and the new ‘Pharmacy Collect’ service provides an additional route to regular testing, making it as easy as possible for people without COVID-19 symptoms to access testing twice a week.

The Pharmacy Collect service is available to people aged over 18 without symptoms, who are able to visit a participating local pharmacy and collect a box of 7 rapid tests to use twice a week at home.

Alongside the rollout of the vaccine, testing will form a crucial part of everyday life as parts of society reopen.

Full detail: [9 in 10 pharmacies now offering free, rapid coronavirus (COVID-19) tests](https://www.gov.uk/government/news/9-in-10-pharmacies-now-offering-free-rapid-coronavirus-covid-19-tests)

**Title:** What do we know about airborne transmission of SARS-CoV-2?

BMJ | 2021; 373: n1030 | 22nd April 2021

How covid-19 spreads is one of the most debated questions of the pandemic. This BMJ briefing explains what the evidence tells us about airborne transmission of the virus, and asks:

* What does airborne transmission mean?
* Is covid-19 airborne?
* What does WHO say about airborne transmission of covid-19?
* What do national governments say about airborne transmission of covid-19?
* How can we prevent airborne transmission?
* Do masks prevent airborne transmission?
* How does airborne transmission compare outdoors versus indoors?

Full detail: [What do we know about airborne transmission of SARS-CoV-2?](https://www.bmj.com/content/373/bmj.n1030)

**Title:** Indoor Air Changes and Potential Implications for SARS-CoV-2 Transmission

JAMA | 16th April 2021

This JAMA Insights review summarizes basic measures of indoor air ventilation as a means to explain how increases in frequency of air exchange and filtration capture efficiency could mitigate far-field airborne transmission of SARS-CoV-2 inside rooms and buildings.

Full detail: [Indoor air changes and potential implications for SARS-CoV-2 transmission](https://jamanetwork.com/journals/jama/fullarticle/2779062)

**Title:** Unusual blood clots are “very rare side effect” of Janssen vaccine, says EMA

BMJ | 2021; 373: n1046 | 21st April 2021

A possible link exists between very rare cases of unusual blood clots with low blood platelets and the Janssen (Johnson & Johnson) covid-19 vaccine, but the benefits still outweigh the risks, the European Medicines Agency (EMA) has said.

The EMA’s Pharmacovigilance Risk Assessment Committee has reviewed all available evidence including eight cases reported in the US, one of which had a fatal outcome. As of 13 April 2021 over seven million people had received Janssen’s one dose vaccine in the US. A warning about the clots will be added to the product information, describing them as a “very rare side effect.”

This comes after the EMA investigated similar cases in people who had received the Oxford-AstraZeneca covid-19 vaccine and concluded that the blood clots with low blood platelets were a “possible” and “extremely rare” side effect. Both vaccines use adenovirus vectors.

Full detail: [Unusual blood clots are “very rare side effect” of Janssen vaccine, says EMA](https://www.bmj.com/content/373/bmj.n1046)

**Title:** Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19

New England Journal of Medicine | 21st April 2021

Ad26.COV2.S is a replication-incompetent human adenovirus 26 containing the gene sequence that produces SARS-CoV-2 spike protein in a prefusion-stabilized conformation.

In this randomized trial involving nearly 40,000 persons, vaccine efficacy was 66% against infection and 85% against severe–critical Covid-19. Efficacy against the variant first identified in South Africa was 64% against moderate disease and 82% against severe–critical disease.

Full article: [Safety and efficacy of single-dose Ad26.COV2.S vaccine against Covid-19](https://www.nejm.org/doi/pdf/10.1056/NEJMoa2101544?articleTools=true)

**Title:** Safety and immunogenicity of SARS-CoV-2 recombinant protein vaccine formulations in healthy adults

The Lancet Infectious Diseases | 19th April 2021

CoV2 preS dTM is a stabilised pre-fusion spike protein vaccine produced in a baculovirus expression system being developed against SARS-CoV-2. This paper presents interim safety and immunogenicity results of the first-in-human study of the CoV2 preS dTM vaccine with two different adjuvant formulations.

The study concludes that lower than expected immune responses, especially in the older age groups, and the high reactogenicity after dose two were probably due to higher than anticipated host-cell protein content and lower than planned antigen doses in the formulations tested, which was discovered during characterisation studies on the final bulk drug substance. Further development of the AS03-adjuvanted candidate vaccine will focus on identifying the optimal antigen formulation and dose.

Full article: [Safety and immunogenicity of SARS-CoV-2 recombinant protein vaccine formulations in healthy adults: interim results of a randomised, placebo-controlled, phase 1–2, dose-ranging study](https://www.thelancet.com/action/showPdf?pii=S1473-3099%2821%2900147-X)

**Title:** Safety and immunogenicity of an MF59-adjuvanted spike glycoprotein-clamp vaccine for SARS-CoV-2

The Lancet Infectious Diseases | 19th April 2021

Given the scale of the ongoing COVID-19 pandemic, the development of vaccines based on different platforms is essential, particularly in light of emerging viral variants, the absence of information on vaccine-induced immune durability, and potential paediatric use.

This study aimed to assess the safety and immunogenicity of an MF59-adjuvanted subunit vaccine for COVID-19 based on recombinant SARS-CoV-2 spike glycoprotein stabilised in a pre-fusion conformation by a novel molecular clamp (spike glycoprotein-clamp [sclamp]).

This first-in-human trial shows that a subunit vaccine comprising mammalian cell culture-derived, MF59-adjuvanted, molecular clamp-stabilised recombinant spike protein elicits strong immune responses with a promising safety profile. However, the glycoprotein 41 peptide present in the clamp created HIV diagnostic assay interference, a possible barrier to widespread use highlighting the criticality of potential non-spike directed immunogenicity during vaccine development.

Studies are ongoing with alternative molecular clamp trimerisation domains to ameliorate this response.

Full article: [Safety and immunogenicity of an MF59-adjuvanted spike glycoprotein-clamp vaccine for SARS-CoV-2: a randomised, double-blind, placebo-controlled, phase 1 trial](https://www.thelancet.com/action/showPdf?pii=S1473-3099%2821%2900200-0)

**Title:** COVID-19 vaccines: building and maintaining confidence

The Lancet Haematology | May 2021

As COVID-19 vaccines are rolled out globally, the AstraZeneca vaccine (Vaxzevria) continues to be marred in controversy, from its slow and still awaited approval by the US Food and Drug Administration amid concerns about paucity of large-scale trial data from the USA, to safety alerts around the development of rare blood clotting events coupled with thrombocytopenia, particularly cerebral venous sinus thrombosis (CVST) and splanchnic vein thrombosis (SVT).

What is clear, this editorial states, is the evidence for the benefits of all the approved COVID-19 vaccines, including AstraZeneca, for preventing serious COVID-19 and helping nations control the disease.

As the pandemic continues, the enormous undertaking of vaccinating billions of people around the world still poses one of the biggest challenges. Transparent reporting of safety is vital to ensure that public trust in the vaccines is improved and maintained, as we continue with one of the largest global vaccination programmes ever undertaken.

Full editorial: [COVID-19 vaccines: building and maintaining confidence](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026%2821%2900107-1/fulltext)

**Title:** 2021: the beginning of a new era of immunisations?

The Lancet | 24th April 2021

While the world is firmly focused on the efficacy, adverse events, licensing, and roll-out of COVID-19 vaccines, the disruption of and barriers to routine immunisations during the pandemic have garnered much less attention.

World Immunization Week (April 24–30) presents an opportunity to reflect on the state of immunisation efforts for vaccine-preventable diseases, how the COVID-19 pandemic has affected progress, and what lessons can accelerate efforts to prevent diseases through immunisation.

This editorial highlights that whilst much has been achieved through vaccination, with many lives saved and disabilities prevented, vaccine hesitancy remains an important issue to tackle. And without addressing the fundamental underlying barriers of inequity, poverty, political posturing, and commercial interest protection, the next decade will not achieve much more than the past.

Full editorial: [2021: the beginning of a new era of immunisations?](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2821%2900900-4/fulltext)

Related: . [World Immunization Week](https://www.who.int/campaigns/world-immunization-week/2021)

**Title:** Rethinking vaccine hesitancy among minority groups

The Lancet | 21st April 2021

Supporting vaccine uptake in communities that have already been disproportionately affected by COVID-19 is an equity issue and will also help achieve broader population immunity.

This comment piece states that an evidence-based understanding of, and response to, the unique needs of communities with low vaccine uptake will allow policy makers to move beyond focusing on individual choices and help address the underlying causes of low vaccine uptake, including lack of confidence in vaccines and health-care services and governments services more broadly, as well as issues related to convenience of access.

Full detail: [Rethinking vaccine hesitancy among minority groups](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2821%2900938-7/fulltext)

**Title:** Infections fell by 65% after first dose of Astra Zeneca or Pfizer vaccine, data show

BMJ | 2021; 373: n1068 | 23rd April 2021

Infections of SARS-CoV-2 fell by 65% after a first dose of the Oxford-AstraZeneca or Pfizer-BioNTech vaccines, preliminary results from a large UK surveillance study indicate. Reductions increased to 70% after a second dose of the Pfizer vaccine, data from the UK Covid-19 Infection Survey show. Not enough people had yet received two doses of the AstraZeneca vaccine to assess this.

The survey, carried out by the University of Oxford in partnership with the Office for National Statistics and the Department of Health and Social Care for England, included data from 1.7 million self-reported swab test results taken from 370 000 UK adults between 1 December 2020 and 3 April 2021.

The results, published in two preprint papers,show that two doses of the Pfizer vaccine offered levels of protection against covid-19 that were similar to levels from previous SARS-CoV-2 infection.

The benefits seem from the vaccines were similar in people over 75 and under 75 and in those with or without long term health conditions, the study found.

The researchers also found no evidence that the AstraZeneca and Pfizer vaccines differed in their ability to reduce infection rates, despite them leading to slightly different immune responses.

Further detail: [Infections fell by 65% after first dose of Astra Zeneca or Pfizer vaccine, data show](https://www.bmj.com/content/373/bmj.n1068)

Research papers:

* [Impact of vaccination on SARS-CoV-2 cases in the community: a population-based study](https://www.ndm.ox.ac.uk/files/coronavirus/ciscommunityvaccinationpaper20210417complete.pdf)

[using the UK’s COVID-19 Infection Survey](https://www.ndm.ox.ac.uk/files/coronavirus/ciscommunityvaccinationpaper20210417complete.pdf)

* [The impact of SARS-CoV-2 vaccines on antibody responses in the general population in the United Kingdom](https://www.ndm.ox.ac.uk/files/coronavirus/covid-19-infection-survey/cisantibodyresponseaftervaccination20210416complete.pdf)

See also: [One Covid vaccine cuts infection rate in all age groups](https://www.bbc.co.uk/news/health-56844220) | BBC News

**Title:** Vaccine Breakthrough Infections with SARS-CoV-2 Variants

New England Journal of Medicine | 21st April 2021

Emerging variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are of clinical concern. In a cohort of 417 persons who had received the second dose of BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) vaccine at least 2 weeks previously, the authors of this brief report identified 2 women with vaccine breakthrough infection.

Despite evidence of vaccine efficacy in both women, symptoms of coronavirus disease 2019 developed, and they tested positive for SARS-CoV-2 by polymerase-chain-reaction testing. Viral sequencing revealed variants of likely clinical importance, including E484K in 1 woman and three mutations (T95I, del142–144, and D614G) in both.

These observations indicate a potential risk of illness after successful vaccination and subsequent infection with variant virus, and they provide support for continued efforts to prevent and diagnose infection and to characterize variants in vaccinated persons.

Full paper: [Vaccine breakthrough infections with SARS-CoV-2 variants](https://www.nejm.org/doi/pdf/10.1056/NEJMoa2105000?articleTools=true)

**workforce wellbeing**

**Title:** Is the UK heading towards mandatory vaccination of healthcare workers?

BMJ | 2021; 373: n1056 | 21st April 2021

This article discusses the possibility of mandatory vaccination of healthcare workers, and asks:

* Why is mandatory vaccination in the news?
* What about care homes?
* But isn’t vaccine uptake high among healthcare workers?
* Would it be legal to mandate vaccination?
* What other vaccines do NHS staff need to have?
* Is there a precedent with the hepatitis B jab?
* What if staff refuse the recommended vaccines?
* Could individual trusts make the covid jab mandatory?
* What’s happening internationally?
* Is mandatory covid vaccination for healthcare workers likely?

Full article: [Is the UK heading towards mandatory vaccination of healthcare workers?](https://www.bmj.com/content/373/bmj.n1056)

**Title:** Navigating Attacks Against Health Care Workers in the COVID-19 Era

JAMA | 21st April 2021

During the pandemic, a variety of situations appear to have promoted attacks against health care workers. A National Nurses United survey in late 2020 of more than 15 000 US registered nurses showed that about 20% of participants said they faced increased on-the-job violence, which they attributed to COVID-19–related staffing shortages, changes in their patient population, and restrictions for visitors.

This Medical News article discusses attacks against health care workers since the COVID-19 pandemic began and ways to prevent some of these incidents.

Full detail: [Navigating attacks against health care workers in the Covid-19 era](https://jamanetwork.com/journals/jama/fullarticle/2779310)

**Health management**

**Title:** Recovering the NHS backlog in some places could take up to five years: bold transformative approach needed

NHS Providers | 18th April 2021

NHS Providers says trusts are getting a clearer picture of the scale of the backlog confronting the health service, and the situation is very concerning.

The organisation which represents every NHS hospital, mental health, community and ambulance service in England says while the overall impact of COVID-19 on NHS waiting times is still emerging, early planning in the worst affected areas shows that, on current trajectories, tackling the problem could take three to five years.

Full detail: [Recovering the NHS backlog in some places could take up to five years: bold transformative approach needed](https://nhsproviders.org/news-blogs/news/recovering-the-nhs-backlog-in-some-places-could-take-up-to-five-years-bold-transformative-approach-needed)

**Title:** Invest to staff the NHS properly, healthcare leaders warn prime minister

BMJ | 2021; 373: n1059 | 21st April 2021

In a joint letter to the prime minister, healthcare leaders have called for a plan, matched by investment, to tackle NHS staff shortages in the medium and long term.

The NHS Confederation, NHS Providers, the British Medical Association, the Royal College of Nursing, the Academy of Royal Medical Colleges, and Unison warned that, without such a plan, vacancies would pose a huge risk to the retention of existing staff.

The letter also highlighted the failure of the NHS people plan, published last July, to tackle four key issues:

* The workforce requirements for delivering the NHS Long Term Plan in each geographical area in the NHS
* The areas of greatest risk and greatest need across the NHS workforce both in terms of service delivery and roles
* The educational, training, and infrastructure costs of increasing supply and the timescales for increasing supply
* The respective roles of international and domestic markets.

Full detail: [Invest to staff the NHS properly, healthcare leaders warn prime minister](https://www.bmj.com/content/373/bmj.n1059?hwsamljwt=eyJ0eXAiOiJKV1QiLCJhbGciOiJIUzI1NiJ9.eyJodHRwczovL3NjaGVtYS5oaWdod2lyZXByZXNzLmNvbS9zYW1sL2F0dHJpYnV0ZS9wZXJzaXN0ZW50LWlkIjpbImh0dHBzOi8vaWRwLmVuZy5uaHMudWsvb3BlbmF0aGVucyFodHRwczovL29wZW5hdGhlbnMtc3AuYm1qLmNvbS9lbnRpdHkvYm1qIWkyajBkcHJ0czFxbWJjY2E1aWYybDVnYyJdLCJzdWIiOiJibWpqb3VybmFscy83NTAyNTkiLCJodHRwczovL3NjaGVtYS5oaWdod2lyZXByZXNzLmNvbS9zYW1sL2F0dHJpYnV0ZS9TaGliLUF1dGhlbnRpY2F0aW9uLUluc3RhbnQiOlsiMjAyMS0wNC0yMlQxMzo0NzowNi42NTZaIl0sImh0dHBzOi8vc2NoZW1hLmhpZ2h3aXJlcHJlc3MuY29tL3NhbWwvc2NvcGUiOlsiNDMxNTkyMi5lbmcubmhzLnVrIl0sImh0dHBzOi8vc2NoZW1hLmhpZ2h3aXJlcHJlc3MuY29tL3NhbWwvaHdQdWJTdWJkYiI6ImJtampvdXJuYWxzIiwiaHR0cHM6Ly9zY2hlbWEuaGlnaHdpcmVwcmVzcy5jb20vc2FtbC9od1B1YlVzZXJJZHMiOlsiNzUwMjU5Il0sImlzcyI6Imh0dHBzOi8vaGlnaHdpcmVwcmVzcy5jb20vIiwiaHR0cHM6Ly9zY2hlbWEuaGlnaHdpcmVwcmVzcy5jb20vc2FtbC9hdHRyaWJ1dGUvU2hpYi1BcHBsaWNhdGlvbi1JRCI6WyJibWoiXSwiaHR0cHM6Ly9zY2hlbWEuaGlnaHdpcmVwcmVzcy5jb20vc2FtbC9hdHRyaWJ1dGUvU2hpYi1BdXRobkNvbnRleHQtRGVjbCI6WyJ1cm46b2FzaXM6bmFtZXM6dGM6U0FNTDoyLjA6YWM6Y2xhc3Nlczp1bnNwZWNpZmllZCJdLCJodHRwczovL3NjaGVtYS5oaWdod2lyZXByZXNzLmNvbS9zYW1sL2F0dHJpYnV0ZS9lZHVQZXJzb25TY29wZWRBZmZpbGlhdGlvbiI6WyJtZW1iZXJANDMxNTkyMi5lbmcubmhzLnVrIl0sImF1ZCI6Imh0dHBzOi8vaGlnaHdpcmVwcmVzcy5jb20vIiwiaHR0cHM6Ly9zY2hlbWEuaGlnaHdpcmVwcmVzcy5jb20vc2FtbC9hdHRyaWJ1dGUvU2hpYi1TZXNzaW9uLUlEIjpbIl83OGY5YzQwZjNkNzNjYzQxN2FmYzU3YTAwNGI1OGNiNyJdLCJodHRwczovL3NjaGVtYS5oaWdod2lyZXByZXNzLmNvbS9zYW1sL2F0dHJpYnV0ZS91c2VybmFtZSI6WyJuaHNzeWFjYXJyaWNrMDAxIl0sImh0dHBzOi8vc2NoZW1hLmhpZ2h3aXJlcHJlc3MuY29tL3NhbWwvYXR0cmlidXRlL29yZ2FuaXNhdGlvbk51bSI6WyI0MzE1OTIyIl0sImh0dHBzOi8vc2NoZW1hLmhpZ2h3aXJlcHJlc3MuY29tL3NhbWwvYXR0cmlidXRlL1NoaWItSWRlbnRpdHktUHJvdmlkZXIiOlsiaHR0cHM6Ly9pZHAuZW5nLm5ocy51ay9vcGVuYXRoZW5zIl0sImV4cCI6MTYxOTE4NTYyNywiaWF0IjoxNjE5MDEyODI3LCJqdGkiOiIxNzY3MjYwZi1kMDMwLTQ0ZjctOTcyYS1jNjIzNzM5MzU1N2EifQ.Z0A95rVAX26_M0R44TomJ92a4j38f9g2HLO8qe_kt-Q)

[Letter to the prime minister NHS workforce](https://i.emlfiles4.com/cmpdoc/7/9/6/1/1/3/files/13830_letter-to-the-prime-minister---nhs-workforce.pdf) | NHS Confederation.

**other**

**Title:** Higher fatality from COVID-19 in patients with cancer in the UK than in Europe

The Lancet Oncology | 22nd April 2021

Echoing concerns expressed by oncologists early in the COVID-19 pandemic, a study led by researchers from Imperial College London (London, UK) has reported that the survival of patients with cancer after infection with SARS-CoV-2 seems to be disparate between the UK and countries in continental Europe, with apparently more detrimental outcomes for patients in the UK compared with their European counterparts.

Further detail: [Higher fatality from COVID-19 in patients with cancer in the UK than in Europe](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045%2821%2900248-5/fulltext)

Related research: [Determinants of enhanced vulnerability to COVID-19 in UK cancer patients: a European Study](https://www.ejcancer.com/article/S0959-8049%2821%2900202-1/fulltext)

**Title:** Mental health and social interactions of older people with physical disabilities in England during the COVID-19 pandemic

The Lancet Public Health | 21st April 2021

The COVID-19 pandemic has affected mental health, psychological wellbeing, and social interactions. People with physical disabilities might be particularly likely to be negatively affected, but evidence is scarce. The aim of this paper was to evaluate the emotional and social experience of older people with physical disabilities during the early months of the COVID-19 pandemic in England.

The authors foud that people with physical disability might be at particular risk for emotional distress, poor quality of life, and low wellbeing during the COVID-19 pandemic, highlighting the need for additional support and targeted mental health services.

Full article: [Mental health and social interactions of older people with physical disabilities in England during the COVID-19 pandemic](https://www.thelancet.com/action/showPdf?pii=S2468-2667%2821%2900069-4)

See also: [Are older people with disabilities neglected in the COVID-19 pandemic?](https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667%2821%2900077-3/fulltext) | The Lancet Public Health

We

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