COVID-19 weekly update

3rd July 2022

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**clinical management**

**title:** How long does SARS-CoV-2 stay in the body?

BMJ | 28TH JUNE 2022

What happens to SARS-CoV-2 when it enters the body, and how long does it linger? Nearly three years since the virus was first discovered, this is still a mystery. Chris Stokel-Walker asks what science has learnt so far…
<https://www.bmj.com/content/377/bmj.o1555/rr>

**title:** Frail older people and those in deprived areas remain at risk from covid-19, even after vaccination [practice alert]

BMJ| 4th JULY 2022

Vaccination against COVID-19 is highly successful at reducing severe illness and death in the population, but people still get infected after vaccination. New research also shows that frail older people, and those who live in deprived areas, are more at risk of infection after vaccination than other groups. The researchers urge family and friends to remain cautious around these vulnerable groups of people…
<https://www.bmj.com/content/378/bmj.o1313#:~:text=The%20study%20also%20shows%20that,when%20they%20encounter%20the%20virus>.

**title:** Analysis of COVID-19–Related Croup and SARS-CoV-2 Variant Predominance in the US

jama|1st july 2022

Recent reports have found an association between SARS-CoV-2 and croup.1-3 We aimed to investigate whether SARS-CoV-2 variants were associated with the proportion of children with croup, as well as hospital and intensive care unit (ICU) admissions and racemic epinephrine (RE) treatment.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2793808>

**title:** Association of Kidney Comorbidities and Acute Kidney Failure With Unfavorable Outcomes After COVID-19 in Individuals With the Sickle Cell Trait

JAMA internal medicine| 27th june 2022

Question Is the presence of sickle cell trait (SCT) associated with worse outcomes of COVID-19?

Findings In this genetic association study of 2729 persons with SCT and 129 848 who were SCT negative, individuals with SCT had a number of preexisting kidney conditions that were associated with unfavorable outcomes following COVID-19. The presence of SCT was associated with increased risk of mortality and acute kidney failure following COVID-19.

Meaning Results strongly support the inclusion of SCT as an adverse prognostic factor for COVID-19.
<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2793722>

**title:** 2022 international clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer, including patients with COVID-19

The Lancet oncology| 21st june 2022

The International Initiative on Thrombosis and Cancer is an independent academic working group of experts aimed at establishing global consensus for the treatment and prophylaxis of cancer-associated thrombosis. The 2013, 2016, and 2019 International Initiative on Thrombosis and Cancer clinical practice guidelines have been made available through a free, web-based mobile phone application. The 2022 clinical practice guidelines, which are based on a literature review up to Jan 1, 2022, include guidance for patients with cancer and with COVID-19. Key recommendations (grade 1A or 1B) include: (1) low-molecular-weight heparins (LMWHs) for the initial (first 10 days) treatment and maintenance treatment of cancer-associated thrombosis; (2) direct oral anticoagulants for the initial treatment and maintenance treatment of cancer-associated thrombosis in patients who are not at high risk of gastrointestinal or genitourinary bleeding, in the absence of strong drug–drug interactions or of gastrointestinal absorption impairment; (3) LMWHs or direct oral anticoagulants for a minimum of 6 months to treat cancer-associated thrombosis; (4) extended prophylaxis (4 weeks) with LMWHs to prevent postoperative venous thromboembolism after major abdominopelvic surgery in patients not at high risk of bleeding; and (5) primary prophylaxis of venous thromboembolism with LMWHs or direct oral anticoagulants (rivaroxaban or apixaban) in ambulatory patients with locally advanced or metastatic pancreatic cancer who are treated with anticancer therapy and have a low risk of bleeding.
[https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(22)00160-7/fulltext](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045%2822%2900160-7/fulltext)

**title:** COVID-19, haemophagocytic lymphohistiocytosis, and infection-induced cytokine storm syndromes

The Lancet infectious diseases| 1st july 2022

We welcome the Grand Round by Danielle Steed and colleagues1 describing bartonella-associated haemophagocytic lymphohistiocytosis in an immunosuppressed patient. This paper highlights the broader topic of infection-induced cytokine storm syndromes. Recent research in COVID-19 cytokine storm syndrome and Castleman disease has expanded the concept of pathological immune activation and established important principles applicable to other infection-induced cytokine storms.2
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00348-6/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900348-6/fulltext)

**title:** Characteristics associated with the residual risk of severe COVID-19 after a complete vaccination schedule: A cohort study of 28 million people in France

The Lancet Regional Health – Europe| 30th june 2022

Prior to the availability of vaccines, the risk factors for developing severe forms of COVID-19 were mostly older age and various comorbidities such as diabetes, cardiovascular diseases, mental disorders, transplantations, and kidney disease. Although vaccines have been shown to be highly effective in preventing severe forms of COVID-19, a residual risk may persist, despite vaccination, for certain population groups.

The study was based on data from the national COVID-19 vaccination database (VAC-SI) coupled with the National Health Data System (SNDS), which contains comprehensive reimbursement and hospitalisation data for all of France. All people fully vaccinated by July 31, 2021, with a double-injection vaccine, i.e., the mRNA BNT162b2, mRNA-1273, or ChAdOx1 nCoV-19 vaccines, or a single dose for people with a previous confirmed SARS-CoV-2 infection were included and followed until August 31, 2021…

…Although vaccination has dramatically reduced the occurrence of severe forms of COVID-19, a residual risk remains for the elderly, immunocompromised, and polypathological populations and warrants complementary preventive measures.
[https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00135-1/fulltext](https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762%2822%2900135-1/fulltext)

**title:** Risk and severity of SARS-CoV-2 reinfections during 2020–2022 in Vojvodina, Serbia: A population-level observational study

The Lancet Regional Health – Europe| 30th june 2022

Data on the rate and severity of SARS-CoV-2 reinfections in real-world settings are scarce and the effects of vaccine boosters on reinfection risk are unknown.

In a population-level observational study, registered SARS-CoV-2 laboratory-confirmed Vojvodina residents, between March 6, 2020 and October 31, 2021, were followed for reinfection ≥90 days after primary infection.

SARS-CoV-2 reinfections were uncommon until the end of 2021 but became common with the advent of Omicron. Very few reinfections were severe. Boosters may modestly reduce reinfection risk.
[https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00147-8/fulltext](https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762%2822%2900147-8/fulltext)

**title:** Recapitulating infection, thermal sensitivity and antiviral treatment of seasonal coronaviruses in human airway organoids

The Lancet ebio medicine | 29th june 2022

Human seasonal coronaviruses usually cause mild upper-respiratory tract infection, but severe complications can occur in specific populations. Research into seasonal coronaviruses is limited and robust experimental models are largely lacking. This study aims to establish human airway organoids (hAOs)-based systems for seasonal coronavirus infection and to demonstrate their applications in studying virus-host interactions and therapeutic development.
[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00313-9/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964%2822%2900313-9/fulltext)

**title:** Thromboprophylactic low-molecular-weight heparin versus standard of care in unvaccinated, at-risk outpatients with COVID-19 (ETHIC): an open-label, multicentre, randomised, controlled, phase 3b triaL

The Lancet haematology| 29th june 2022

COVID-19 is associated with inflammation and an increased risk of thromboembolic complications. Prophylactic doses of low-molecular-weight heparin have been used in hospitalised and non-critically ill patients with COVID-19. We aimed to evaluate the efficacy and safety of prophylactic low-molecular-weight heparin (enoxaparin) versus standard of care (no enoxaparin) in at-risk outpatients with COVID-19.

…The ETHIC trial results suggest that prophylaxis with low-molecular-weight heparin had no benefit for at-risk outpatients with COVID-19. Although the trial was terminated early, our data, combined with data from similar studies, provide further insights to inform international guidelines and influence clinical practice.
[https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(22)00173-9/fulltext](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026%2822%2900173-9/fulltext)

**title:** Enoxaparin for primary thromboprophylaxis in symptomatic outpatients with COVID-19 (OVID): a randomised, open-label, parallel-group, multicentre, phase 3 trial

THE LANCET HAEMATOLOGY| 29TH JUNE 2022

The risk of developing long covid is lower among people with the omicron variant of SARS-CoV-2
COVID-19 is a viral prothrombotic respiratory infection. Heparins exert antithrombotic and anti-inflammatory effects, and might have antiviral properties. We aimed to investigate whether thromboprophylaxis with enoxaparin would prevent untoward hospitalisation and death in symptomatic, but clinically stable outpatients with COVID-19…

… These findings suggest thromboprophylaxis with enoxaparin does not reduce early hospitalisations and deaths among outpatients with symptomatic COVID-19. Futility of the treatment under the initial study design assumptions could not be conclusively assessed owing to under-representation of older patients and consequent low event rates.
[https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(22)00175-2/fulltext](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026%2822%2900175-2/fulltext)

**title:** Antithrombotic prophylaxis for symptomatic outpatients with COVID-19: less is consistently more

THE LANCET HAEMATOLOGY| 29TH JUNE 2022

Based on data from 1348 participants enrolled in three randomised trials done in diverse settings, there is no evidence to support routine use of aspirin, factor Xa inhibitors, or LMWH for the prevention of adverse arterial or venous thrombosis, or progression of COVID-19 among symptomatic outpatients with COVID-19. ACTIV-4B, OVID, and ETHIC share not only high degrees of adherence, compliance, and follow-up, but also very low absolute event rates despite being done at times of low or absent vaccination and before the availability of oral agents designed for outpatient use such as nirmatrelvir–ritonavir, which markedly further reduce hospitalisation rates.9 Investigations of the utility of antithrombotic treatments to prevent respiratory failure and mortality in any patient population with SARS-CoV-2 infection have generally shown little if any role for antithrombotics. Thus, in the absence of new data, the bottom line for a global clinical community that continues to deal with a frustrating ongoing pandemic, less consistently appears to be more with regard to antithrombotic therapy for outpatients with COVID-19.
[https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(22)00205-8/fulltext](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026%2822%2900205-8/fulltext)

**title:** IgG N-glycome changes during the course of severe COVID-19: An observational study

The Lancet ebio medicine| 29th june 2022

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) causes a respiratory illness named coronavirus disease 2019 (COVID-19), which is one of the main global health problems since 2019. Glycans attached to the Fc portion of immunoglobulin G (IgG) are important modulators of IgG effector functions. Fc region binds to different receptors on the surface of various immune cells, dictating the type of immune response. Here, we performed a large longitudinal study to determine whether the severity and duration of COVID-19 are associated with altered IgG glycosylation.
[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00282-1/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964%2822%2900282-1/fulltext)

**title:** Multi-ancestry Mendelian randomization of omics traits revealing drug targets of COVID-19 severity

The Lancet ebio medicine| 27th june 2022

Our study identified six proteins as showing putative causal effects on COVID-19 severity. OAS1 and SERPINA1 were targets of existing drugs in trials as potential COVID-19 treatments. ICAM1, ICAM5 and FCRL3 are related to the immune system. Across the six targets, OAS1 has no reliable instrument in African ancestry; SERPINA1, FCRL3, ICAM5 and ENTPD5 showed a different level of putative causal evidence in European and African ancestries, which highlights the importance of more powerful ancestry-specific GWAS and value of multi-ancestry MR in informing the effects of drug targets on COVID-19 across different populations. This study provides a first step towards clinical investigation of beneficial and adverse effects of COVID-19 drug targets.
[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00293-6/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964%2822%2900293-6/fulltext)

**title:** SARS-CoV-2 Infection in Patients with a History of VITT

new england journal of medicine| 27th june 2022

We performed periodic evaluation of VITT antibody status (study registry, EUPAS45098) in a cohort of 69 patients with a history of VITT who had received an adenovirus vector Covid-19 vaccine. Of these patients, 24 did not receive any subsequent doses of a Covid-19 vaccine; the remaining 45 patients received subsequent doses of a messenger RNA (mRNA) vaccine (either the BNT162b2 [Pfizer–BioNTech] or the mRNA-1273 [Moderna] vaccine). Of these patients, 31 received a second dose and 14 received a third dose…
<https://www.nejm.org/doi/full/10.1056/NEJMc2206601#:~:text=Our%20finding%20that%20Covid%2D19,vaccination%20with%20an%20mRNA%20vaccine>.

**title:** Increasing Understanding of SARS-CoV-2 Infection in Young Children—Would They Benefit From Immunization?

JAMA| 27th june 2022

…Kubale et al1 provide clear data indicating that SARS-CoV-2 infects young children more so than older children, adding to the emerging evidence that the youngest children are at risk for hospitalization and negative outcomes after infection. Combined with studies in older children and adults demonstrating that vaccination can provide improved protection even after natural infection and can protect from hospitalization, immunization appears to be a reliable method to protect young children. With the upcoming release of vaccine safety data, regulators can perform a complete risk-benefit analysis, and much-needed protection for our youngest population may be possible.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2793630>

**long-term effects**

**title:** Bridging Knowledge Gaps in the Diagnosis and Management of Neuropsychiatric Sequelae of COVID-19

JAMA PSYCHIATRY| 29th june 2022

Neuropsychiatric symptoms have been reported as a prominent feature of postacute sequelae of COVID-19 (PASC), with common symptoms that include cognitive impairment, sleep difficulties, depression, posttraumatic stress, and substance use disorders. A primary challenge of parsing PASC epidemiology and pathophysiology is the lack of a standard definition of the syndrome, and little is known regarding mechanisms of neuropsychiatric PASC.
<https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2793903>

**title:** Association Between BNT162b2 Vaccination and Long COVID After Infections Not Requiring Hospitalization in Health Care Workers

JAMA| 1st JuLY 2022

In this longitudinal observational study conducted among health care workers with SARS-CoV-2 infections not requiring hospitalization, 2 or 3 doses of vaccine, compared with no vaccination, were associated with lower long COVID prevalence. Study limitations include that symptoms and duration were self-reported, and causality cannot be inferred.
<https://jamanetwork.com/journals/jama/fullarticle/2794072>

**title:** Evidence of previous SARS-CoV-2 infection in seronegative patients with long COVID

the lancet ebio medicine| 27th june 2022

Background. There is currently no consensus on the diagnosis, definition, symptoms, or duration of COVID-19 illness. The diagnostic complexity of Long COVID is compounded in many patients who were or might have been infected with SARS-CoV-2 but not tested during the acute illness and/or are SARS-CoV-2 antibody negative.

Methods. Given the diagnostic conundrum of Long COVID, we set out to investigate SARS-CoV-2-specific T cell responses in patients with confirmed SARS-CoV-2 infection and/or Long COVID from a cohort of mostly non-hospitalised patients.

Findings. We discovered that IL-2 release (but not IFN-γ release) from T cells in response to SARS-CoV-2 peptides is both sensitive (75% +/−13%) and specific (88%+/−7%) for previous SARS-CoV-2 infection >6 months after a positive PCR test. We identified that 42–53% of patients with Long COVID, but without detectable SARS-CoV-2 antibodies, nonetheless have detectable SARS-CoV-2 specific T cell responses.

Interpretation. Our study reveals evidence (detectable T cell mediated IL-2 release) of previous SARS-CoV-2 infection in seronegative patients with Long COVID.
[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00310-3/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964%2822%2900310-3/fulltext)

**title:** Understanding and addressing long-COVID among migrants and ethnic minorities in Europe

THE LANCET regional health europe| 29th june 2022

A wealth of evidence suggests that migrants and ethnic minorities have been disproportionally impacted by COVID-19, in terms of cases, hospitalisations, deaths and mental health outcomes in many European countries.2,3 In addition, emerging data have suggested inequities in the delivery of vaccines to these populations.4 We here describe migrants and ethnic minorities combined because these groups overlap and share common characteristics including socioeconomic and psychosocial vulnerabilities. The term ‘migrants’ is used as an umbrella term encompassing all the different subgroups of people who immigrated including asylum seekers, undocumented immigrants etc. The extent to which migrants and ethnic minorities are impacted by long-COVID is, however, not known, despite an increasing literature identifying a number of relevant risk factors for long-COVID including older age, disease severity, comorbidities and admission to Intensive Care Units.
[https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00121-1/fulltext](https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762%2822%2900121-1/fulltext)

**rates & variants**

**title:** Covid-19: Sharp rise in infections seen across the UK

BMJ| 4th july 2022

Covid-19 infections in the UK are up 32% on the previous week with an estimated 2.3 million people infected, according to the Office for National Statistics (ONS).

Rates have continued to increase across all four UK countries, likely driven by the growth of the BA.4 and BA.5 omicron subvariants, the ONS said.

In the week ending 25 June an estimated 1 829 100 people would have tested positive for covid in England—around one in 30 people—according to the ONS coronavirus infection survey. A week earlier that rate was one in 40.

The rates are even higher in Scotland with an estimated 288 200 people testing positive, equating to one in 18 people.

The data, published on 1 July, show that in Wales an estimated 106 000 people tested positive, or around one in 30. In Northern Ireland the estimated number of people testing positive was 7000 or one in 25…
<https://www.bmj.com/content/378/bmj.o1638#:~:text=The%20overall%20hospital%20admission%20rate,at%20the%20start%20of%20June>.

**title:** Clinical severity of omicron lineage BA.2 infection compared with BA.1 infection in South Africa

The Lancet | 30th june 2022

Similar to BA.1, BA.2 is associated with substantial loss in neutralising activity in individuals infected with wild-type SARS-CoV-2 or recipients of mRNA vaccines.3 BA.2 has also been associated with increased transmissibility compared with BA.1,4 and in England was shown to have an increased growth rate compared with BA.1.5 However, data are lacking on the clinical severity of the BA.2 lineage compared with BA.1. We aimed to assess the severity of BA.2 infections compared with BA.1 in South Africa…
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00981-3/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2900981-3/fulltext)

**title:** Augmented neutralisation resistance of emerging omicron subvariants BA.2.12.1, BA.4, and BA.5

the lancet infectious diseases| 28th june 2022

The SARS-CoV-2 omicron (B.1.1.529) variant is highly resistant against antibody-mediated neutralisation due to many mutations in the spike (S) protein.1 Several omicron subvariants have been detected, with BA.2.12.1 (first detected in the USA) and BA.4 and BA.5 (first detected in South Africa) currently outcompeting the previously circulating BA.1 and BA.2 subvariants in several countries. The S proteins of BA.4 and BA.5, which are identical on the protein level, and BA.2.12.1 harbour unique mutations (appendix pp 1–2), but it is largely unknown whether they differ from BA.1 and BA.2 regarding neutralisation sensitivity.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00422-4/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900422-4/fulltext)

**infection control**

**title:** Airborne SARS-CoV-2

BMJ | 29th june 2022

 Time for an indoor air revolution

Debate over the exact mode of transmission of SARS-CoV-2 has been intense.1 This is entirely reasonable, given that the mechanism of spread determines preventive and potentially lifesaving policies. But the choice between respiratory aerosol or droplet settled on short range droplets, which neatly circumvented any risk outside the fabled 2m zone.1 This choice gave rise to social distancing, hand and surface hygiene, and masks, but not to improved indoor air quality.

And so the debate smoulders on, as Duval and colleagues (doi:10.1136/bmj-2021-068743) report from their linked systematic review supporting the role of long distance airborne transmission of SARS-CoV-2.2 The review examined covid-19 transmission events in a variety of indoor community settings ranging from fitness facilities, offices, buses, and restaurants to choir venues and a church, but not hospitals, hospices, or care homes.2345678 The inclusion of care home outbreaks might have strengthened overall findings, along with more recent studies detailing nosocomial clusters among vaccinated healthcare workers…
[Airborne SARS-CoV-2 | The BMJ](https://www.bmj.com/content/377/bmj.o1408)

**title:** Immunity and infectivity in covid-19

BMJ |1st july 2022

Pregnant individuals who received a booster dose of the BNT162b2 (Pfizer-BioNTech) COVID-19
The risk of SARS-CoV-2 transmission is greatest just before symptom onset and in the early symptomatic period

There is no surrogate marker to determine infectiousness: PCR positivity overestimates the duration of infectivity and can lead to negative consequences such as delayed surgery, delayed access to health care, and blocking of healthcare systems; culture is not practical; and negative lateral flow tests do not equate exactly with non-infectiousness

Decisions related to transmission risk must take into account all relevant factors, including the overall risk of infection in the community, the individual’s ability to comply with prevention measures, their home and work environment, and the risk profile of their likely future close contacts..
<https://www.bmj.com/content/378/bmj-2020-061402>

**title:** Long distance airborne transmission of SARS-CoV-2: rapid systematic review

BMJ| 29th june 2022

This rapid systematic review found evidence suggesting that long distance airborne transmission of SARS-CoV-2 might occur in indoor settings such as restaurants, workplaces, and venues for choirs, and identified factors such as insufficient air replacement that probably contributed to transmission. These results strengthen the need for mitigation measures in indoor settings, particularly the use of adequate ventilation.
<https://www.bmj.com/content/377/bmj-2021-068743>

**title:** Duration of Shedding of Culturable Virus in SARS-CoV-2 Omicron (BA.1) Infection

new england journal of medicine| 29th june 2022

…Our data suggest that some persons who are infected with the omicron and delta SARS-CoV-2 variants shed culturable virus more than 5 days after symptom onset or an initial positive test.
<https://www.nejm.org/doi/full/10.1056/NEJMc2202092#:~:text=Our%20data%20suggest%20that%20some,Caitlin%20Marino%2C%20B.S.&text=James%20Regan%2C%20B.S>.

**title:** Intrinsic generation time of the SARS-CoV-2 Omicron variant: An observational study of household transmission

the lancet regional health europe| 30th june 2022

Starting from the final months of 2021, the SARS-CoV-2 Omicron variant expanded globally, swiftly replacing Delta, the variant that was dominant at the time. Many uncertainties remain about the epidemiology of Omicron; here, we aim to estimate its generation time…

…We estimated a mean intrinsic generation time of 6.84 days (95% credible intervals, CrI, 5.72–8.60), and a mean realized household generation time of 3.59 days (95%CrI: 3.55–3.60). The household serial interval was 2.38 days (95%CrI 2.30–2.47) with about 51% (95%CrI 45–56%) of infections caused by symptomatic individuals being generated before symptom onset.

Interpretation. These results indicate that the intrinsic generation time of the SARS-CoV-2 Omicron variant might not have shortened as compared to previous estimates on ancestral lineages, Alpha and Delta, in the same geographic setting. Like for previous lineages, pre-symptomatic transmission appears to play a key role for Omicron transmission. Estimates in this study may be useful to design quarantine, isolation and contact tracing protocols and to support surveillance (e.g., for the accurate computation of reproduction numbers).
[https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00140-5/fulltext#:~:text=Findings,CrI%3A%203.55%E2%80%933.60)](https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762%2822%2900140-5/fulltext#:~:text=Findings,CrI%3A%203.55%E2%80%933.60)).

**title:** Effectiveness of BNT162b2 vaccine against SARS-CoV-2 infection and severe COVID-19 in children aged 5–11 years in Italy: a retrospective analysis of January–April, 2022

the lancet| 30th june 2022

 Background. By April 13, 2022, more than 4 months after the approval of BNT162b2 (Pfizer–BioNTech) for children, less than 40% of 5–11-year-olds in Italy had been vaccinated against COVID-19. Estimating how effective vaccination is in 5–11-year-olds in the current epidemiological context dominated by the omicron variant (B.1.1.529) is important to inform public health bodies in defining vaccination policies and strategies…

…Interpretation. Vaccination against COVID-19 in children aged 5–11 years in Italy showed a lower effectiveness in preventing SARS-CoV-2 infection and severe COVID-19 than in individuals aged 12 years and older. Effectiveness against infection appears to decrease after completion of the current primary vaccination cycle.
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01185-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2901185-0/fulltext)

Linked commentary: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01245-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2901245-4/fulltext)

**title:** BNT162b2 VACCINE EFFECTIVENESS AGAINST OMICRON IN CHILDREN 5 TO 11 YEARS OF AGE

new england journal of medicine| 29th june 2022

This observational study of effectiveness of the BNT162b2 vaccine among children 5 to 11 years of age showed a vaccine effectiveness of 51% against documented SARS-CoV-2 infection and 48% against symptomatic Covid-19 at 7 to 21 days after the second dose. Our results also suggested that effectiveness may be greater among younger children (5 or 6 years of age) than older children (10 or 11 years of age).
<https://www.nejm.org/doi/full/10.1056/NEJMoa2205011#:~:text=This%20observational%20study%20of%20effectiveness,days%20after%20the%20second%20dose>.

**title:** Associations of BMI with COVID-19 vaccine uptake, vaccine effectiveness, and risk of severe COVID-19 outcomes after vaccination in England: a population-based cohort study

the lancet diabetes & endocrinology| 30th june 2022

Background A high BMI has been associated with a reduced immune response to vaccination against influenza. We aimed to investigate the association between BMI and COVID-19 vaccine uptake, vaccine effectiveness, and risk of severe COVID-19 outcomes after vaccination by using a large, representative population-based cohort from England.tion Do rates of reported myocarditis or pericarditis following COVID-19 mRNA vaccination…

…Interpretation Using BMI categories, there is evidence of protection against severe COVID-19 in people with overweight or obesity who have been vaccinated, which was of a similar magnitude to that of people of healthy weight. Vaccine effectiveness was slightly lower in people with underweight, in whom vaccine uptake was also the lowest for all ages. In the vaccinated cohort, there were increased risks of severe COVID-19 outcomes for people with underweight or obesity compared with the vaccinated population with a healthy weight. These results suggest the need for targeted efforts to increase uptake in people with low BMI (<18·5 kg/m²), in whom uptake is lower and vaccine effectiveness seems to be reduced. Strategies to achieve and maintain a healthy weight should be prioritised at the population level, which could help reduce the burden of COVID-19 disease.
[https://www.thelancet.com/pdfs/journals/landia/PIIS2213-8587(22)00158-9.pdf](https://www.thelancet.com/pdfs/journals/landia/PIIS2213-8587%2822%2900158-9.pdf)
[Linked commentary](https://www.thelancet.com/journals/landia/article/PIIS2213-8587%2822%2900170-X/fulltext#:~:text=the%20protection%20of%20COVID%2D19,against%20those%20who%20were%20unvaccinated.)

**title:** The Vaccine-Hesitant Moment

new england journal of medicine| 29th june 2022

Timing is everything regarding both the personal moment and the historical moment when it comes to making a decision about vaccination. The uncertainty and constantly evolving nature of the Covid-19 pandemic and response measures, the rapid introduction of new vaccines, emerging variants, and the volatility of the surrounding politics and polarization have all contributed to public questioning and the trends in vaccine hesitancy.
<https://www.nejm.org/doi/full/10.1056/NEJMra2106441>

**title:** Immunogenicity and Safety of Beta-Adjuvanted Recombinant Booster Vaccine

new england journal of medicine| 29th june 2022

…Over the short term, heterologous boosting with the beta-adjuvanted MVB.1.351 vaccine resulted in a higher neutralizing-antibody response against the beta variant as well as against the original strain and the delta and omicron BA.1 variants than did the mRNA vaccine BNT162b2 or the MVD614 formulation. The use of new vaccines that contain beta spike protein may be an interesting strategy for broader protection against SARS-CoV-2 variants.
<https://www.nejm.org/doi/full/10.1056/NEJMc2206711>

**title:** Observed protection against SARS-CoV-2 reinfection following a primary infection: A Danish cohort study among unvaccinated using two years of nationwide PCR-test data

the lancet regional health europe| 30th june 2022

SARS-CoV-2 infection offered a high level of sustained protection against reinfection, comparable with that offered by vaccines, but decreased with the introduction of new main virus variants; dramatically so when Omicron appeared. Protection was lower among the elderly but appeared more pronounced following symptomatic compared to asymptomatic infections. The level of estimated protection against serious disease was somewhat higher than that against infection and possibly longer lasting. Decreases in protection against reinfection, seemed primarily to be driven by viral evolution.
[https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00146-6/fulltext](https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762%2822%2900146-6/fulltext)

**title:** Heterologous booster response after inactivated virus BBIBP-CorV vaccination in older people

the lancet infectious diseases| 28th june 2022

Few data are available on effectiveness of a booster dose for individuals who are immunised with inactivated COVID-19 vaccines.2 The results presented here indicate that a heterologous booster dose with ChAdOx1 nCoV-19, Sputnik V, or BNT162b2 vaccines markedly increases the neutralising activity against the omicron variant in older people who have received two doses of BBIBP-CorV.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00427-3/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900427-3/fulltext)

**title:** Effect of a 2-week interruption in methotrexate treatment versus continued treatment on COVID-19 booster vaccine immunity in adults with inflammatory conditions (VROOM study): a randomised, open label, superiority trial

the lancet respiratory medicine| 27th june 2022

To our knowledge, this study was the first randomised trial of interrupting methotrexate treatment around the time of vaccination with additional COVID-19 vaccine doses in people that had received at least two previous vaccinations against COVID-19. The study showed that a 2-week interruption of methotrexate treatment immediately after COVID-19 booster vaccination resulted in a 2·19-fold increase in the S1-RBD antibody response after 4 weeks. The enhanced antibody response was maintained at 12 weeks. The treatment effect was present across groups of varying ages, methotrexate doses, diseases, and history of SARS-CoV-2 infection. Interrupting methotrexate for 2 weeks did not affect quality of life or general health. There was a temporary deterioration in self-reported disease activity and disease control at 4 weeks that resolved by week 12. More participants in the suspend methotrexate group than in the continue methotrexate group self-reported disease flare-up in the first 4 weeks, but most self-managed with no appreciable difference in seeking health-care input for flares across the two groups.
[https://www.thelancet.com/pdfs/journals/lanres/PIIS2213-2600(22)00186-2.pdf](https://www.thelancet.com/pdfs/journals/lanres/PIIS2213-2600%2822%2900186-2.pdf)

**title:** Improving COVID-19 vaccine immunogenicity by interrupting methotrexate treatment

the lancet respiratory medicine| 27th june 2022

…In summary, this important study shows that a 2-week interruption of methotrexate after booster COVID-19 vaccination results in increased immunogenicity compared with no interruption among patients with several immune-mediated inflammatory diseases.
[https://www.thelancet.com/pdfs/journals/lanres/PIIS2213-2600(22)00224-7.pdf](https://www.thelancet.com/pdfs/journals/lanres/PIIS2213-2600%2822%2900224-7.pdf)
[Linked BMJ commentary](https://www.bmj.com/content/377/bmj.o1586#:~:text=News-,Covid%2D19%3A%20Pausing%20immune%20suppressing%20drugs%20enhances%20antibody,response%20to%20boosters%2C%20study%20shows&text=Interrupting%20methotrexate%20treatment%20for%20two,new%20research1%20has%20shown.)

**title:** An exploratory analysis of the response to ChAdOx1 nCoV-19 (AZD1222) vaccine in males and females

the lancet ebio medicine| 29th june 2022

Our results show that there is no evidence of difference in efficacy of the COVID-19 vaccine ChAdOx1 nCoV-19 in males and females. Greater reactogenicity in females was not associated with any difference in vaccine efficacy.
[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00309-7/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964%2822%2900309-7/fulltext)

**title:** COVID-19 vaccination antibody responses in patients with aplastic anaemia and paroxysmal nocturnal haemoglobinuria

the lancet haematology| 30th june 2022

Our data highlight the importance of at least two vaccinations in patients with PNH or a history of aplastic anaemia to achieve a good SARS-CoV-2 antibody response, and we expect that they will benefit from booster programmes. Although we have found robust antibody levels after two vaccinations, further studies are needed to determine the longevity of response, degree of effective IgG responses, T-cell responses, and long-term infection outcomes.
[https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(22)00183-1/fulltext](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026%2822%2900183-1/fulltext)

**title:** Association of SARS-CoV-2 Seropositivity and Symptomatic Reinfection in Children in Nicaragua

JAMA| 27th june 2022

Question What is the burden of COVID-19 among young children, and how does risk of reinfection vary with age?

Findings In this cohort study of 1964 children in Nicaragua aged 0 to 14 years, children younger than 2 years had the highest rates of symptomatic and severe COVID-19, particularly compared with children aged 5 to 14 years.

Meaning These findings suggest that the burden of COVID-19 and associated severe illness may not be evenly distributed across age groups in children.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2793625#:~:text=Another%20study32%20in%20Nicaragua,we%20observed%20in%20our%20study>.

**title:** Shifting gender barriers in immunisation in the COVID-19 pandemic response and beyond

the lancet | 2nd july 2022

Before the COVID-19 pandemic, gender-related vaccine coverage challenges affected child populations with low and zero vaccine coverage.1 Similarly, women were less likely than men to receive relevant or trustworthy vaccine information because of literacy, education, and digital gaps. Women were also less likely to get vaccinated because of work and domestic care obligations. Compared with men, women had less trust in vaccines, were less able to make health-care decisions because of limited household decision-making power, and had greater difficulty reaching vaccination sites because of limited mobility…
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01189-8/fulltext?rss=yes](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2901189-8/fulltext?rss=yes)

**health management**

**title:** Comparison of trends in Clostridioides difficile infections in hospitalised patients during the first and second waves of the COVID-19 pandemic: A retrospective sentinel surveillance study

the lancet refional health europe| 27th june 2022

Background. During the COVID-19 pandemic, several factors, such as improved hand hygiene, social distancing, and restricted hospital referral, may have had an influence on the epidemiology of Clostridioides difficile infections (CDI).

Methods. The annual CDI incidence rate of nine hospitals participating in the Dutch sentinel CI surveillance with complete data was compared between 2020 and the previous five surveillance years. Trends in characteristics of hospitalised CDI patients in 21–24 participating hospitals were compared between the first (March 13–May 12, 2020) or second Dutch COVID-19 wave (September 17, 2020-January 1, 2021) and the same calendar periods in 2015 through 2019. All analyses were adjusted for trend changes over time.

Findings. The annual CDI incidence rate in 2020 was lower compared to previous years. During the second wave, the percentage of CDI patients with severe CDI was higher compared to earlier (25·8% in 2020 vs 17·9% in 2015-2019 (RR 1·6; 95%CI 1·1-2·3)). After adjustment for delayed C. difficile diagnostics (≥8 days from start symptoms), the increase disappeared. Delayed C. difficile diagnostics was indeed more common during the second wave (RR 1·7; 95%CI 1·1-2·6), but only for community-onset CDI (CO-CDI).

Interpretation. This study shows that a higher percentage of severe CDI cases was observed during the second COVID-19 wave. This may partially be caused by delayed diagnostics, potentially due to decreased visits to a physician or restricted hospital referral for CO-CDI patients.
[https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00118-1/fulltext](https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762%2822%2900118-1/fulltext)

**recovery**

**title:** Searching for SARS-CoV-2 origins: the saga continues

the lancet microbe | july 2022

On June 9, the first preliminary report of the Scientific Advisory Group for the Origins of Novel Pathogens (SAGO) was published, representing the work of the group so far in distilling the questions that need to be asked to understand the origins of the COVID-19 pandemic and future pandemics. Given the ongoing nature of this work, it is likely to evolve as information is uncovered and new gaps are identified, just as all scientific enquiries should. However, this open-ended approach does create an opportunity for political interference at some level…
[https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(22)00161-6/fulltext](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247%2822%2900161-6/fulltext)

**title:** A new paradigm is needed for financing the pandemic fund

the lancet| 29th june 2022

…Today, another round of innovation is needed to address the future challenges of a post-pandemic, climate emergency world. However, we believe that the World Bank's 2022 white paper outlining how the proposed PPR FIF will work2 is a step back to the donor-driven past that even the funds of 20 years ago were trying to escape. Without a radical rethink, the crucial global public good of PPR will not receive the sustainable funding it needs.
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01239-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2901239-9/fulltext)

**title:** Assessment of Resilience Training for Hospital Employees in the Era of COVID-19

BMJ| 1st july 2022

Question Is a group-coaching program designed to reduce stress and teach resilience skills feasible, acceptable, and preliminarily useful for health care workers during the COVID-19 pandemic?

Findings In this pilot cohort study of 153 health care workers and hospital employees from a single health system, the group-coaching program was feasible and acceptable, as demonstrated by high demand, retention, and satisfaction. Measured according to validated scales, self-reported resilience, stress, anxiety, and burnout improved among participants.

Meaning Results of this study suggest that resilience-building programs may support improved mental health outcomes.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2793802>

**title:** Association of Nonpharmaceutical Interventions During the COVID-19 Pandemic With Invasive Pneumococcal Disease, Pneumococcal Carriage, and Respiratory Viral Infections Among Children in France

JAMA | 28th june 2022

Question Was the implementation of nonpharmaceutical interventions (NPIs) during the COVID-19 pandemic associated with changes in the incidence of invasive pneumococcal disease (IPD) and associated pneumococcal carriage and respiratory viral infections (RSVs) in children in France?

Findings In this cohort study using interrupted time series analysis of data from multiple national surveillance systems involving 11 944 children, the incidence of pediatric IPD decreased after implementation of NPIs during the COVID-19 pandemic. This decrease was associated with decreases in influenza and RSV cases, but the pneumococcal carriage rate remained stable.

Meaning These results suggest that the established association between pneumococcal carriage and IPD was modified after viral epidemiological changes associated with NPIs, suggesting that interventions targeting respiratory viruses may help prevent a large proportion of pediatric IPD cases.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2793638>

Linked commentary: <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2793641>

**public health & health inequalities**

**title:** Adverse SARS-CoV-2-associated outcomes among people experiencing social marginalisation and psychiatric vulnerability: A population-based cohort study among 4,4 million people

the lancet regional health europe | 29th june 2022

Knowledge of the adverse problems related to SARS-CoV-2 infection in marginalised and deprived groups may help to prioritise more preventive efforts in these groups. We examined adverse outcomes associated with SARS-CoV-2 infection among vulnerable segments of society.

Methods. Using health and administrative registers, a population-based cohort study of 4.4 million Danes aged at least 15 years from 27 February 2020 to 15 October 2021 was performed. People with 1) low educational level, 2) homelessness, 3) imprisonment, 4) substance abuse, 5) supported psychiatric housing, 6) psychiatric admission, and 7) severe mental illness were main exposure groups. Chronic medical conditions were included for comparison. COVID-19-related outcomes were: 1) hospitalisation, 2) intensive care, 3) 60-day mortality, and 4) overall mortality. PCR-confirmed SARS-CoV-2 infection and PCR-testing were also studied. Poisson regression analysis was used to compute adjusted incidence and mortality rate ratios (IRRs, MRRs)…

…Interpretation. Socially marginalised and psychiatrically vulnerable individuals had substantially elevated risks of adverse health outcomes following SARS-CoV-2 infection. The results highlight that pandemic preparedness should address inequalities in health, including infection prevention and vaccination of vulnerable groups.
[https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00115-6/fulltext](https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762%2822%2900115-6/fulltext)

**international perspectives**

**title:** Covid-19: Canada outperformed comparable nations in pandemic response, study reports

BMJ|30th june 2022

1 month ago, North Korea declared its first COVID-19 cases. Information is scare, but the outbreak
Canada performed better than the majority of G10 countries in its response to the first two years of the covid-19 pandemic, a study has concluded.

A paper published in the Canadian Medical Association Journal concluded that Canadians were better vaccinated than comparable western countries, with fewer infections, fewer covid deaths, and lower mortality from all causes.1

Researchers from the University of Toronto, some of whom are members of Ontario’s covid-19 science advisory board, linked the country’s lower death rate to the persistence of its social restrictions and the relative lack of antivaccine sentiment.

The study compared responses from the 11 countries in the G10, comprising Canada, Belgium, France, Germany, Italy, Japan, the Netherlands, Sweden, Switzerland, the UK, and the US. Japan was an extreme outlier, with by far the fewest deaths and infections despite having the oldest population and imposing the mildest restrictions.

Canada was the next best in health outcomes, being the only country of the remaining 10 to record fewer than 100 000 infections per million population from the pandemic’s outset to February 2022. Canada saw 82 700 cases per million people, while the worst hit countries were France with 312 000 per million and the Netherlands with 313 000 per million. Japan reported only 27 600 cases per million…
[Covid-19: Canada outperformed comparable nations in pandemic response, study reports | The BMJ](https://www.bmj.com/content/377/bmj.o1615#:~:text=News-,Covid%2D19%3A%20Canada%20outperformed%20comparable%20nations,in%20pandemic%20response%2C%20study%20reports&text=Canada%20performed%20better%20than%20the,pandemic%2C%20a%20study%20has%20concluded.)

We

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

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

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