COVID-19 weekly update

7th April 2022

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**clinical management**

**title:** Thromboembolism and bleeding after covid-19

bmj| 6th april 2022

Risks are increased even after mild infections

It is now clear from meta-analyses of case series,12 cohort studies,3 and self-controlled case series that the risk of venous thromboembolism is increased after SARS-CoV-2 infection. However, two important questions remain: for how long post-infection is the risk increased, and does mild infection also increase risk? In a linked paper, Katsoularis and colleagues (doi:10.1136/bmj-2021-069590) address these questions by applying two complementary study designs to data from several Swedish registries. The authors identified more than one million people with laboratory confirmed SARS-CoV-2 infection from the start of the pandemic to mid-2021, matched on age, sex, and county of residence to more than four million people who had not had a positive SARS-CoV-2 test result. After adjustment for a wide range of potential confounders, the authors reported a fivefold increase in risk of deep vein thrombosis (relative incidence 4.98, 95% confidence interval 4.96 to 5.01), 33-fold increase in risk of pulmonary embolism (33.05, 32.8 to 33.3), and an almost twofold increase in risk of bleeding (1.88, 1.71 to 2.07) in the 30 days after infection.

The results were largely consistent in alternative analyses using a self-controlled case series approach comparing risk 1-30 days after the infection with a control period. The advantage of this approach is that comparing two periods in the same individual eliminates confounding by factors that are stable over time, such as genetics. The large study population enabled novel, granular analyses. Previous studies have already shown that the association between SARS-CoV2-2 and thromboembolic events is much stronger for pulmonary embolism than for deep vein thrombosis.8 Katsoularis and colleagues were able to show that the increased risk of thromboembolism also lasts longer for pulmonary embolism than for deep vein thrombosis; six and three months, respectively.

These authors also report an increased risk of bleeding after SARS-CoV-2 infection that is consistent with previous studies. Use of thromboprophylaxis after SARS-CoV-2 infection clearly carries a risk of bleeding. However, covid-19 has also been associated with coagulopathy and disseminated intravascular coagulation.9 Although unable to identify the underlying mechanism, the authors show that the association with bleeding is independent of anticoagulation before SARS-CoV-2 infection and lasts for two months after infection.

Since risks of thromboembolism and bleeding were highest among participants with more severe covid-19, vaccination could reduce the overall risk both by preventing infection and by reducing its severity when it does occur. While risk of thromboembolic events is increased after vaccination,510 the magnitude of risk remains smaller and persists for a shorter period that that associated with infection.

Are the new study findings still relevant now that nearly 65% of the world’s population has received at least one vaccine dose11? Yes—current vaccines are highly effective against severe covid-19 but confer only moderate protection against infection with the omicron variant.1213 Breakthrough infections are common, even after a third dose,14 and effectiveness against symptomatic disease appears to decrease to less than 50% 10 weeks after vaccination.13

Although many infections with the omicron variant are mild, the new study confirms an increased risk of venous thromboembolism even among those with milder infections who do not require admission to hospital.4 The association was much weaker (relative incidence 5.87, 95% confidence interval 4.88 to 7.05 for pulmonary embolism) than that among patients admitted to hospital (64.49, 53.91 to 77.15) and those admitted to intensive care (196.98, 128.71 to 301.46), but mild disease accounts for a much larger proportion of infections (94.5% in this study). This patient group may therefore contribute a substantial number of thromboembolic events.

A study from England15 reported a doubling in the incidence of, and mortality from, thromboembolism since the start of the pandemic in 2020 compared with the same periods in 2018 and 2019. The same study reported comparable increases among individuals without positive SARS-CoV-2 test results. Some of those without a positive test result will have been infected before widespread testing was available, but others will have had mild or asymptomatic infections.16

Despite the potential for new variants of concern, most governments are removing restrictions and shifting their focus to determining how best to “live with covid.”17 Katsoularis and colleagues’ study reminds us of the need to remain vigilant to the complications associated with even mild SARS-CoV-2 infection, including thromboembolism.
<https://www.bmj.com/content/377/bmj.o817>

**title:** Risks of deep vein thrombosis, pulmonary embolism, and bleeding after covid-19: nationwide self-controlled cases series and matched cohort study

bmj| 6th april 2022

Objective To quantify the risk of deep vein thrombosis, pulmonary embolism, and bleeding after covid-19. Design Self-controlled case series and matched cohort study. Setting National registries in Sweden.

Participants 1 057 174 people who tested positive for SARS-CoV-2 between 1 February 2020 and 25 May 2021 in Sweden, matched on age, sex, and county of residence to 4 076 342 control participants.

Main outcomes measures Self-controlled case series and conditional Poisson regression were used to determine the incidence rate ratio and risk ratio with corresponding 95% confidence intervals for a first deep vein thrombosis, pulmonary embolism, or bleeding event. In the self-controlled case series, the incidence rate ratios for first time outcomes after covid-19 were determined using set time intervals and the spline model. The risk ratios for first time and all events were determined during days 1-30 after covid-19 or index date using the matched cohort study, and adjusting for potential confounders (comorbidities, cancer, surgery, long term anticoagulation treatment, previous venous thromboembolism, or previous bleeding event).

Results Compared with the control period, incidence rate ratios were significantly increased 70 days after covid-19 for deep vein thrombosis, 110 days for pulmonary embolism, and 60 days for bleeding. In particular, incidence rate ratios for a first pulmonary embolism were 36.17 (95% confidence interval 31.55 to 41.47) during the first week after covid-19 and 46.40 (40.61 to 53.02) during the second week. Incidence rate ratios during days 1-30 after covid-19 were 5.90 (5.12 to 6.80) for deep vein thrombosis, 31.59 (27.99 to 35.63) for pulmonary embolism, and 2.48 (2.30 to 2.68) for bleeding. Similarly, the risk ratios during days 1-30 after covid-19 were 4.98 (4.96 to 5.01) for deep vein thrombosis, 33.05 (32.8 to 33.3) for pulmonary embolism, and 1.88 (1.71 to 2.07) for bleeding, after adjusting for the effect of potential confounders. The rate ratios were highest in patients with critical covid-19 and highest during the first pandemic wave in Sweden compared with the second and third waves. In the same period, the absolute risk among patients with covid-19 was 0.039% (401 events) for deep vein thrombosis, 0.17% (1761 events) for pulmonary embolism, and 0.101% (1002 events) for bleeding.

Conclusions The findings of this study suggest that covid-19 is a risk factor for deep vein thrombosis, pulmonary embolism, and bleeding. These results could impact recommendations on diagnostic and prophylactic strategies against venous thromboembolism after covid-19.
<https://www.bmj.com/content/377/bmj-2021-069590>

**title:** The self-controlled case series method and covid-19

bmj| 6th april 2022

The self-controlled case series method is one of two approaches used to estimate the association between covid-19 and venous thromboembolism or bleeding. This article briefly describes the method, its assumptions, and how it was implemented in the linked study, and offers some pointers to guide the interpretation of the results.
<https://www.bmj.com/content/377/bmj.o625>

**title:** Pulse Oximetry for Monitoring Patients with Covid-19 at Home — A Pragmatic, Randomized Trial

bmj| 6th april 2022

Reports of silent hypoxia in patients with coronavirus disease 2019 (Covid-19) have raised the question of whether patients should use pulse oximeters at home to measure oxygen saturation rather than relying on subjective dyspnea as an indicator of clinical deterioration.1,2 Many Covid-19 remote-monitoring programs include home pulse oximetry,3,4 but the effectiveness of these programs remains unknown. We report the findings from a randomized trial that assessed a text message–based remote-monitoring program (COVID Watch) supplemented with monitoring of oxygen saturation by means of a home pulse oximeter. As part of routine care in our six-hospital health system (which includes more than 500 outpatient practices), adults in our electronic health record with Covid-19 infection — as determined by their clinician or a confirmed positive test for Covid-19 — are enrolled in COVID Watch, a 2-week program involving twice-daily automated text messages inquiring about dyspnea and offering rapid callbacks from nurses when appropriate. This program has been associated with improved survival as compared with no remote monitoring.5

From November 29, 2020, to February 5, 2021, we randomly assigned in a 1:1 ratio patients who were enrolled in COVID Watch to participate in the standard monitoring program in addition to home pulse oximetry or the standard program alone. Patients in the pulse oximetry group were provided a pulse oximeter and were monitored for subjective symptoms or a low or declining oxygen saturation. Ethical considerations precluded assigning patients to no monitoring as a control. The prespecified primary outcome was the number of days the patient was alive and out of the hospital at 30 days, assessed in patients with test-confirmed Covid-19. Exploratory outcomes included patient-reported anxiety levels, use of health care services, and death at 30 days. Details regarding the patients and the trial methods are provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org; the trial protocol is also available at NEJM.org…

…Among patients with Covid-19, the addition of home pulse oximetry to remote monitoring did not result in a greater number of days alive and out of the hospital than subjective assessments of dyspnea alone.
<https://www.nejm.org/doi/full/10.1056/NEJMc2201541?query=featured_coronavirus>

**title:** Fluvoxamine for Outpatient Management of COVID-19 to Prevent Hospitalization: A Systematic Review and Meta-analysis

jama network open| 6th april 2022

Question Is early administration of fluvoxamine associated with hospitalization in symptomatic adult outpatients with confirmed COVID-19?

Findings In this systematic review and bayesian meta-analysis of 3 clinical trials, which accounted for varying prior probabilities coupled with a frequentist sensitivity analysis, there was a high probability (94.1%-98.6%) that fluvoxamine was associated with a reduced risk for hospitalization, with a frequentist risk ratio of 0.75 (95% CI, 0.58-0.97).

Meaning These findings suggest that fluvoxamine, a widely available and inexpensive treatment for outpatients with COVID-19, was associated with a reduction in hospitalizations.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790742>

**title:** Estimated Health Outcomes and Costs Associated With Use of Monoclonal Antibodies for Prevention or Mitigation of SARS-CoV-2 Infections

jama network open| 5th april 2022

Mass vaccination against COVID-19 has limited hospitalizations and deaths associated with the disease, but even in countries with excess supply of vaccines, substantial numbers of people remain unvaccinated and at risk of severe disease. The experience of high-income countries, such as Israel and Singapore, shows that serious illnesses requiring oxygen supplementation and intensive care will persist even as vaccination rates reach 80% of the population.1

Anti–SARS-CoV-2 monoclonal antibodies, including REGEN-COV (casirivimab and imdevimab), have been shown to prevent infection in household contacts2 and decrease risk of hospitalization or death related to COVID-19.3 Beyond the benefits to the individual, use of these treatments may also preserve scarce medical resources during outbreaks. Questions remain concerning whether monoclonal antibodies would best be used as prophylaxis, treatment, or a combination of prophylaxis and treatment. Therefore, we aimed to (1) assess potential health and cost benefits associated with using REGEN-COV as postexposure prophylaxis (PEP) in household contacts and for treating COVID-19 and (2) help policy makers with decisions about prioritization of REGEN-COV while supply is limited, using Singapore as a case study.

Methods. The report of this economic evaluation follows the CHEERS reporting guideline. Our research involved the analysis of routinely collected, aggregated data for public health policy making, and ethical approval was not required, as advised by the Departmental Ethics Review Committee of the Saw Swee Hock School of Public Health at the National University of Singapore.

We identified 14 scenarios (eFigure in the Supplement) in which REGEN-COV was allocated to different groups of individuals at increased risk stratified by age, vaccination status, and source of infection (ie, household vs nonhousehold). Epidemiological and clinical characteristics of patients with COVID-19 were collated by the Ministry of Health and National Centre for Infectious Diseases of Singapore (eAppendix and eTables 1-3 in the Supplement).

Health outcomes included the number of patients with severe illnesses requiring oxygen supplementation, patients with critical illness admitted to the intensive care units, deaths due to COVID-19, and disability-adjusted life-years (DALYs). Economic outcomes were the overall cost of PEP and treatment with REGEN-COV, cost of hospitalization, and cost per DALY averted. We calculated net costs by subtracting baseline cost without REGEN-COV (ie, the status quo) from total cost with REGEN-COV. We performed sensitivity analyses by setting the relative risk reduction (RRR) of REGEN-COV to 31.6% and 87.1% (ie, the 95% CI bounds) instead of the point estimate of 70.4%.3 All analyses were conducted between September 2 and September 29, 2021.

Results. All scenarios considered were cost-effective using the threshold of 1.15 gross national income4 per DALY; some were cost-saving. Treating recently diagnosed individuals and those aged 60 years and older with REGEN-COV was the most cost-saving, with a net cost saving of approximately US $340 000 for every 10 000 infections (Table). Using REGEN-COV as PEP in individuals exposed to infected family members was less cost-effective compared with using it to treat only infected individuals (cost saving of US $19 500 vs US $1200). Because all scenarios in which there were sufficient supplies were cost-effective, we considered which scenarios were most robust to the risk of exhausting supplies amid an epidemic wave. Preserving REGEN-COV for treatment of individuals aged 60 years and older was associated with the greatest decrease in DALYs and severe illnesses across a range of supply scenarios, although in scenarios with few available doses, use should be restricted to older individuals (ie, those ≥70 years) (Figure). In sensitivity analyses, our results were robust to changes in RRR, with all scenarios remaining cost-effective.

Discussion. These findings suggest that in high-income settings, adults aged 60 years and older who are not fully vaccinated should be given priority to receive REGEN-COV for treating recently diagnosed COVID-19, particularly when supply is limited. It should be noted, however, that clinical trials on the use of REGEN-COV as PEP2 or for treatment3 were conducted before widespread circulation of the SARS-CoV-2 Delta and Omicron variants; therefore, a limitation of this analysis is that the estimated cost-effectiveness may be influenced if the efficacy of REGEN-COV differs by variant. Care must be taken to prevent the availability of monoclonal antibodies from deterring vaccination, which should remain the preferred means of preventing severe COVID-19.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790706>

**title:** Implementation of Clinical Practice Guidelines for Hospitalized Patients With COVID-19 in Academic Medical Centers

jama network open| 4th april 2022

COVID-19 management has evolved rapidly, creating challenges for implementation. This study was conducted to assess the fidelity with which academic medical centers (AMCs) adopted evidence into practice.

Methods. This survey study was deemed exempt from review and informed consent by the University of California, San Francisco, because it does not involve human participants. Response rates were computed according to the American Association for Public Opinion Research (AAPOR) reporting guideline.

We surveyed members of the Hospital Medicine Reengineering Network (Figure 1)1 from December 17, 2020, to February 10, 2021, and compared their institutional recommendations for COVID-19 management with available evidence at that time from pivotal randomized clinical trials (RCTs) (eAppendix in the Supplement) and guidelines from the National Institutes of Health,2 Infectious Diseases Society of America,3 and American Society of Hematology.4 Data were analyzed from February 10 to March 4, 2021.

Results. Of 83 hospitals contacted, 52 (63%) responded. Hospitalist leaders involved in the direct care of patients with COVID-19 provided responses. A total of 49 sites (94%) self-identified as AMCs; the remaining 3 sites (6%) identified as AMC-affiliated teaching hospitals. Fifty-one sites (98%) issued internal COVID-19 management guidance. Guidance at 48 sites (94%) was generated by multidisciplinary committees, including infectious disease (47 sites [98%]), infection control (43 sites [90%]), hospital medicine (42 sites [88%]), and critical care (40 sites [83%]). Of 51 sites with internal COVID-19 management guidance, recommendations were disseminated most commonly through email (43 sites [84%]), institutional websites (42 sites [82%]), and integration into the electronic health record as COVID-19-specific order sets (37 sites [73%]) and note templates (33 sites [65%]). The percentage of institutions recommending each studied intervention is shown in Figure 2, alongside simplified RCT findings and guidelines. Notable results include 94% to 100% of sites recommending dexamethasone for patients requiring at least 4 L of oxygen, 69% recommending remdesivir for patients receiving mechanical ventilation, 81% recommending dexamethasone for patients requiring 1 to 2 L of oxygen, 67% implementing awake proning, 35% limiting remdesivir use to the “early or viral phase of illness,” and 17% recommending D-dimer–based therapeutic anticoagulation. The proportion of sites recommending each intervention varied from a low of 10% for convalescent plasma for patients without antibodies to 100% for dexamethasone in patients requiring mechanical ventilation.

Discussion. In this survey study, 3 themes emerged from our analysis. First, translation from evidence to practice guidelines was remarkably complete for interventions supported by aligned national guidelines and high-quality studies. A striking example is the near universal adoption of dexamethasone among patients requiring at least 4 L of supplementary oxygen only 6 to 8 months after the RECOVERY trial demonstrated a survival benefit. The lone exception to this trend was baricitinib; however, new evidence and guidelines were released within 1 week of survey distribution. Practice convergence was also observed when evidence and guidelines aligned against interventions, as seen in the infrequent recommendation of dexamethasone for patients with oxygen saturation greater than 94%, as measured by pulse oximetry. However, clear opportunity for improvement still exists.

Second, institutions favored treatment over not treatment, particularly when guidelines diverged from each other or from the underlying evidence, as exemplified by 69% to 81% of sites recommending remdesivir or dexamethasone, respectively, when evidence or guidelines conflicted. We suspect this finding reflects systemic biases to do something rather than nothing when faced with uncertainty, likely exacerbated by inconsistent definitions of disease severity across studies and guidelines.

Finally, AMCs demonstrated a willingness to innovate across a range of interventions. Novel interventions, such as awake proning, phase-of-illness–restricted remdesivir, and D-dimer–based therapeutic anticoagulation, varied widely with respect to patient selection and procedural specifics, but collectively, and with 17% to 67% of sites recommending 1 or more of such novel interventions, they demonstrate that AMCs were sophisticated consumers of information, willing to bridge knowledge gaps with expert opinion. Additional research is needed to understand how AMCs monitor innovation outcomes and deimplement practices when negative evidence emerges.

Limitations of this study include a 37% nonresponse rate, reliance on self-reporting, lack of longitudinal follow-up, and lack of data on actual clinical practice and outcomes. Nonetheless, our findings demonstrate that AMCs were capable of responding nimbly to emerging data and shifting guidelines, although both overtreatment and experimentation were observed where significant uncertainty persisted. While factors unique to the early pandemic likely shaped this performance, we hope some strategies, such as use of focused multidisciplinary teams and novel information sharing tools, can be harnessed to accelerate the translation of evidence to bedside for COVID-19 and beyond.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790619>

**Title:** Definition, diagnosis, and management of COVID-19-associated pulmonary mucormycosis: Delphi consensus statement from the Fungal Infection Study Forum and Academy of Pulmonary Sciences, India

the lancet infectious diseases| 4th april 2022

Using a modified Delphi method, we have formulated a consensus statement for the diagnosis and management of CAPM. We selected 26 experts from various disciplines who are involved in managing CAPM. Three rounds of the Delphi process were held to reach consensus (≥70% agreement or disagreement) or dissensus. A consensus was achieved for 84 of the 89 statements. Pulmonary mucormycosis occurring within 3 months of COVID-19 diagnosis was labelled CAPM and classified further as proven, probable, and possible. We recommend flexible bronchoscopy to enable early diagnosis. The experts proposed definitions to categorise dual infections with aspergillosis and mucormycosis in patients with COVID-19. We recommend liposomal amphotericin B (5 mg/kg per day) and early surgery as central to the management of mucormycosis in patients with COVID-19. We recommend response assessment at 4–6 weeks using clinical and imaging parameters. Posaconazole or isavuconazole was recommended as maintenance therapy following initial response, but no consensus was reached for the duration of treatment. In patients with stable or progressive disease, the experts recommended salvage therapy with posaconazole or isavuconazole. CAPM is a rare but under-reported complication of COVID-19. Although we have proposed recommendations for defining, diagnosing, and managing CAPM, more extensive research is required.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00124-4/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900124-4/fulltext)

**Title:** Implementation of corticosteroids in treatment of COVID-19 in the ISARIC WHO Clinical Characterisation Protocol UK: prospective, cohort study

the lancet digital health| 1st april 2022

Dexamethasone was the first intervention proven to reduce mortality in patients with COVID-19 being treated in hospital. We aimed to evaluate the adoption of corticosteroids in the treatment of COVID-19 in the UK after the RECOVERY trial publication on June 16, 2020, and to identify discrepancies in care.

Methods. We did an audit of clinical implementation of corticosteroids in a prospective, observational, cohort study in 237 UK acute care hospitals between March 16, 2020, and April 14, 2021, restricted to patients aged 18 years or older with proven or high likelihood of COVID-19, who received supplementary oxygen. The primary outcome was administration of dexamethasone, prednisolone, hydrocortisone, or methylprednisolone. This study is registered with ISRCTN, ISRCTN66726260.

Findings. Between June 17, 2020, and April 14, 2021, 47 795 (75·2%) of 63 525 of patients on supplementary oxygen received corticosteroids, higher among patients requiring critical care than in those who received ward care (11 185 [86·6%] of 12 909 vs 36 415 [72·4%] of 50 278). Patients 50 years or older were significantly less likely to receive corticosteroids than those younger than 50 years (adjusted odds ratio 0·79 [95% CI 0·70–0·89], p=0·0001, for 70–79 years; 0·52 [0·46–0·58], p<0·0001, for >80 years), independent of patient demographics and illness severity. 84 (54·2%) of 155 pregnant women received corticosteroids. Rates of corticosteroid administration increased from 27·5% in the week before June 16, 2020, to 75–80% in January, 2021.

Interpretation. Implementation of corticosteroids into clinical practice in the UK for patients with COVID-19 has been successful, but not universal. Patients older than 70 years, independent of illness severity, chronic neurological disease, and dementia, were less likely to receive corticosteroids than those who were younger, as were pregnant women. This could reflect appropriate clinical decision making, but the possibility of inequitable access to life-saving care should be considered.
[https://www.thelancet.com/journals/landig/article/PIIS2589-7500(22)00018-8/fulltext](https://www.thelancet.com/journals/landig/article/PIIS2589-7500%2822%2900018-8/fulltext)

**Title:** Incidence Rates and Clinical Outcomes of SARS-CoV-2 Infection With the Omicron and Delta Variants in Children Younger Than 5 Years in the US

jama pediatrics| 1st april 2022

…At the surgery, we’re doing our best to support the patients we know about by monitoring the
With the Omicron variant (B.1.1.529), SARS-CoV-2 infections and hospitalizations reached record levels.1 Children younger than 5 years may be especially vulnerable because they are not eligible for COVID-19 vaccination.2 We examined incidence rates and clinical outcomes of Omicron infection before and after Omicron became the predominant variant in the US.

Methods. This cohort study (September 1, 2021-January 31, 2022) was approved by the MetroHealth System institutional review board (IRB); the need for informed consent was waived owing to use of deidentified patient data. We used the TriNetX Analytics Platform to access aggregated and deidentified electronic health records of 90 million patients from 66 health care organizations. TriNetX built-in analytic functions permit patient-level analyses while only reporting population-level data. Patients represented 28% of the US population from 50 states covering diverse geographic, age, race, income, and insurance groups.3 Self-identified race and ethnicity were included owing to their association with SARS-CoV-2 infection risk and outcomes.

The study population contained 3 cohorts of children younger than 5 years with no prior SARS-CoV-2 infection: (1) Omicron cohort, who contracted SARS-CoV-2 infection between December 26, 2021, and January 25, 20224; (2) Delta (B.1.617.2) cohort, who contracted SARS-CoV-2 infection between September 1, 2021, and November 15, 20214; and (3) Delta2 cohort, who contracted SARS-CoV-2 infection between November 16 and November 30, 2021.4 Delta2 cohort was developed to control for later time periods and shorter infection window.

We examined monthly incidence rates of SARS-CoV-2 infection (new cases per 1000 persons per day) between September 1, 2021, and January 31, 2022, among children without prior infections, stratified by 2 age groups (0-2 and 3-4 years). We tested whether severe clinical outcomes differed between Omicron and Delta cohorts and between Delta2 and Delta cohorts. Cohorts were propensity-score matched for demographics (Table). Risk of death, emergency department visits, hospitalizations, intensive care unit (ICU) admissions, and the need for mechanical ventilation within 14 days after initial SARS-CoV-2 infection were compared between matched cohorts using hazard ratios (HRs) and 95% CIs. Statistical tests were conducted within the TriNetX Analytics Platform with significance set at a 2-sided P value <.05. TriNetX database and statistical analyses are in the eMethods in the Supplement. This study followed STROBE reporting guidelines.

Results. This cohort study included a total of 651 640 children younger than 5 years: (1) Omicron cohort, 22 772 children; (2) Delta cohort, 66 692 children; and (3) Delta2 cohort, 10 496 children. The monthly incidence rate of SARS-CoV-2 infections was mostly stable (1.0-1.5 cases per 1000 persons per day) between September and November 2021 (Delta-predominant period) but rapidly increased to 2.4 to 5.6 cases per 1000 persons per day in December 2021, coincident with the emergence of Omicron variant. Monthly incidence rate of SARS-CoV-2 infections peaked at 8.6 cases per 1000 persons per day in the first half of January 2022 (Omicron-predominant period) and 8.2 in the second half of January 2022. Incidence rate of Omicron infection was higher in children aged 0 to 2 years than in those aged 3 to 4 years. Omicron cohort was younger and with fewer comorbidities than Delta cohort, but differences were eliminated after matching (Table). Risks for severe clinical outcomes in children infected with Omicron variant were significantly lower than those in the matched Delta cohort (Figure, A), whereas the risks for severe clinical outcomes in Delta2 cohort did not differ from those in Delta cohort (Figure, B). There were fewer than 10 deaths in all cohorts.

Discussion. Results of this cohort study suggest that the incidence rate of SARS-CoV-2 infection with Omicron variant was 6 to 8 times that of Delta variant in children younger than 5 years, but severe clinical outcomes were less frequent than with Delta variant. Study limitations include potential biases introduced by the observational and retrospective analyses of electronic health records and the need for validation of the results from other data. Study findings may inform risk-benefit considerations about in-person school attendance, mask use, and vaccination implementation for young children.
<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2790793>

**title:** Telomere-length dependent T-cell clonal expansion: A model linking ageing to COVID-19 T-cell lymphopenia and mortality

the lancet ebiomedicine| 31st march 2022

Background. Severe COVID-19 T-cell lymphopenia is more common among older adults and entails poor prognosis. Offsetting the decline in T-cell count during COVID-19 demands fast and massive T-cell clonal expansion, which is telomere length (TL)-dependent.

Methods. We developed a model of TL-dependent T-cell clonal expansion capacity with age and virtually examined the relation of T-cell clonal expansion with COVID-19 mortality in the general population.

Findings. The model shows that an individual with average hematopoietic cell TL (HCTL) at age twenty years maintains maximal T-cell clonal expansion capacity until the 6th decade of life when this capacity rapidly declines by more than 90% over the next ten years. The collapse in the T-cell clonal expansion capacity coincides with the steep increase in COVID-19 mortality with age.

Interpretation. Short HCTL might increase vulnerability of many older adults, and some younger individuals with inherently short HCTL, to COVID-19 T-cell lymphopenia and severe disease.
[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00162-1/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964%2822%2900162-1/fulltext)

**rates and variants**

**title:** Covid-19: Infections in England reached record high in March, finds React study

bmj | 6th april 2022

Covid-19 infections in England reached an “unprecedented” level last month, with prevalence higher than at any other time during the pandemic, the Real Time Assessment of Community Transmission (React) monitoring study has reported. Covid-19 prevalence was 6.37% between 8 and 31 March 2022, based on samples from over 100 000 people. This is more than twice the 2.88% in February 2022 and exceeds the previous high of 4.41% recorded in January 2022 during the peak of the first wave of omicron. Of 4038 positive samples that were sequenced in the latest round of the Imperial College London and Ipsos MORI study, most (3035, 89.7%) were the BA.2 subvariant of omicron”.

“We observed unprecedented levels of SARS-CoV-2 infection in England in March 2022 and an almost complete replacement of omicron BA.1 by BA.2,” concluded the study, published as a preprint on 6 April. “The high and increasing prevalence in older adults may increase hospital admissions and deaths despite high levels of vaccination,” it warned.

In the final round of the study, which is ceasing after its funding was withdrawn by the government, 109 459 people swabbed themselves at home, and 6902 samples showed positive when analysed by polymerase chain reaction, yielding a weighted prevalence of 6.37% (95% credible interval (CrI), 6.21% to 6.53%). Prevalence of SARS-CoV-2 infection was increasing overall (reproduction number R=1.07, 95% CrI, 1.06 to 1.09), but the greatest increase was in those aged over 55 years (R=1.12, 95% CrI, 1.09 to 1.14). On 31 March 2022, estimated prevalence among the over 55s was 8.31%, nearly 20 times higher than the average for that age group across the whole period from May 2020 through to March 2022.

Paul Elliott, director of the React programme from Imperial College London’s School of Public Health, told a Science Media Centre briefing that he was concerned about the rising prevalence in older adults. “In children, it seems to have peaked and is turning down. In younger adults, there seems to be a plateauing. But the over 55s seem to be continuing to go up and they are obviously the most vulnerable group. “I think it’s people mixing more but also we know that many older people had their booster back in October and November last year. So, it’s likely that there is some waning of protection against infection, although there is very good protection against severe illness.” But he cautioned, “Hospital admissions with covid-19 in England have been increasing in recent weeks, and clearly ongoing surveillance is required both to monitor severe outcomes of covid-19, but also emergence of new variants.”

Prevalence increased in every region when compared with the previous round of the study, with the highest at 8.13% (95% CrI, 7.59% to 8.71%) in the south west. The decision to remove funding from React means the UK will now solely rely on the covid-19 infection survey by the Office for National Statistics to track prevalence. Elliott said, “Clearly, we’re disappointed that we’re not going to be in the field anymore, but that’s how it is. We’re very pleased that there’s still going to be some surveillance.”
<https://www.bmj.com/content/377/bmj.o905>

**title:** Covid-19: Hospital admissions continue to climb amid record infection rates

bmj | 4th april 2022

The number of patients admitted to hospitals in England with covid-19 has more than doubled in the past month and is continuing to rise amid record infection levels, latest data show. NHS England figures from the seven days ending 27 March show an average of 2008 covid related hospital admissions a day,1 up from 1749 the previous week and 949 in the seven days ending 27 February. Covid related admissions driven by the omicron subvariant BA.2 are now similar to the figure of around 14 000 a week that the NHS saw during the first omicron wave, in early January this year. Deaths are also rising again. In the seven days ending 27 March, 988 people died in UK hospitals with covid, compared with 725 in the week ending 13 March—a rise of 36%. The level of covid-19 infection also reached a record high in England in the most recent week recorded, as 4.9 million people—one in 13—are thought to have been infected in the week ending 26 March, showed data from the Office for National Statistics.3 The prevalence in Scotland is around one in 12, in Wales one in 14, and in Northern Ireland around one in 15.

NHS staff absences. Amid the spiralling infection rates and hospital admissions, the BMA’s deputy chair of council, David Wrigley, urged the government to reconsider its decision to end free testing for most for the population from 1 April. “The number of people with covid is now shockingly high with the most infections we’ve ever seen, and hospitalisations and deaths are also on the rise,” he said. “Right now we’re in a situation where covid is rife across the UK, and yet testing—a simple tool to help people know if they have the infection—is no longer being made free for our patients. This means that as infection rates soar, people don’t know if they are infected and have to self-isolate, and therefore are unable to protect family members and the wider community.”

Hospital bosses are also concerned about the number of NHS staff off work because of covid-19. The number of staff in acute care trusts who were absent from work for covid related reasons rose by almost a fifth (19%) last week, from a seven day average of 23 127 in the week ending 20 March to 27 571 on 27 March.4 Staff absences because of covid have risen by 86% in three weeks since the week ending 6 March.

Miriam Deakin, NHS Providers’ director of policy and strategy, said, “These figures show the NHS is under sustained pressure, with a concerning increase in the number of NHS staff off work because of covid-19. This is a particular worry because of the knock-on effect on patient care, including efforts to tackle care backlogs and the ongoing demand for services.”
<https://www.bmj.com/content/377/bmj.o882>

**infection control**

**title:** Covid-19: UK adds sore throat, headache, fatigue, and six other symptoms to official list

BMJ|4th april 2022

Background. Reinfection after primary SARS-CoV-2 infection is uncommon in adults, but little is
The UK’s official list of covid-19 symptoms1 has been updated to include sore throat, fatigue, headache, and six other symptoms which are now commonly associated with the virus.

Shortness of breath, an aching body, a blocked or runny nose, loss of appetite, diarrhoea, and feeling sick or being sick have also been added to the list on the NHS website. “The symptoms are very similar to symptoms of other illnesses, such as colds and flu,” the website says.

The UK’s official symptom list for covid-19 previously included just three indications—fever, persistent cough, and a loss or change in taste or smell. Yet the World Health Organization, the US Centres for Disease Control and Prevention, and European nations such as Spain and France have all listed a far wider range of symptoms for some time.

Tim Spector, the lead scientist of the Zoe covid-19 symptom tracker app, who told The BMJ last December2 that the UK was an international outlier in limiting its list to three symptoms, said, “Everyone at Zoe is happy to see that the NHS has finally updated the official symptom list after two years of lobbying and contributor input. The addition of more symptoms is a step in the right direction and it could help reduce infections.

“However, while this is good news, I’d like to see the order of the symptoms changed, as the NHS list puts far too much emphasis on symptoms like fever and anosmia, which we know are much less common since the omicron variant emerged. According to the Zoe covid study, the top five symptoms being reported by contributors with a positive covid test are runny nose (83%), fatigue (71%), sore throat (69%), headache (69%), and sneezing (68%).” Spector added, “It seems this decision has been made in light of the changes to testing. We were always told that the barrier to expanding the list was that adding more symptoms could overwhelm testing capacity, so it makes sense that since free testing has now stopped, the list has been updated.”

As far back as last June,3 GPs were urging the government to update the official list of symptoms amid concerns that their patients were confused about what to look for and when to take a covid test. But with the government withdrawing free universal testing for most of the population on 1 April, some experts have argued that the change to the symptom list has come too late. Kit Yates, senior lecturer in the Department for Mathematical Sciences at the University of Bath, said on Twitter, “We’ve been asking for this for over a year and now it’s come too late to be really helpful.”4. The UK Health Security Agency—which has overseen the changes—was approached for a comment but not responded by the time of publication.
<https://www.bmj.com/content/377/bmj.o892>

**title:** Risk of SARS-CoV-2 reinfection and COVID-19 hospitalisation in individuals with natural and hybrid immunity: a retrospective, total population cohort study in Sweden

The Lancet infectious diseases| 31st march 2022

Background. Real-world evidence supporting vaccination against COVID-19 in individuals who have recovered from a previous SARS-CoV-2 infection is sparse. We aimed to investigate the long-term protection from a previous infection (natural immunity) and whether natural immunity plus vaccination (hybrid immunity) was associated with additional protection.

Methods. In this retrospective cohort study, we formed three cohorts using Swedish nationwide registers managed by the Public Health Agency of Sweden, the National Board of Health and Welfare, and Statistics Sweden. Cohort 1 included unvaccinated individuals with natural immunity matched pairwise on birth year and sex to unvaccinated individuals without natural immunity at baseline. Cohort 2 and cohort 3 included individuals vaccinated with one dose (one-dose hybrid immunity) or two doses (two-dose hybrid immunity) of a COVID-19 vaccine, respectively, after a previous infection, matched pairwise on birth year and sex to individuals with natural immunity at baseline. Outcomes of this study were documented SARS-CoV-2 infection from March 20, 2020, until Oct 4, 2021, and inpatient hospitalisation with COVID-19 as main diagnosis from March 30, 2020, until Sept 5, 2021.

Findings. Cohort 1 was comprised of 2 039 106 individuals, cohort 2 962 318 individuals, and cohort 2 and 3 567 810 individuals. During a mean follow-up of 164 days (SD 100), 34 090 individuals with natural immunity in cohort 1 were registered as having had a SARS-CoV-2 reinfection compared with 99 168 infections in non-immune individuals; the numbers of hospitalisations were 3195 and 1976, respectively. After the first 3 months, natural immunity was associated with a 95% lower risk of SARS-CoV-2 infection (adjusted hazard ratio [aHR] 0·05 [95% CI 0·05–0·05] p<0·001) and an 87% (0·13 [0·11–0·16]; p<0·001) lower risk of COVID-19 hospitalisation for up to 20 months of follow-up. During a mean follow-up of 52 days (SD 38) in cohort 2, 639 individuals with one-dose hybrid immunity were registered with a SARS-CoV-2 reinfection, compared with 1662 individuals with natural immunity (numbers of hospitalisations were eight and 113, respectively). One-dose hybrid immunity was associated with a 58% lower risk of SARS-CoV-2 reinfection (aHR 0·42 [95% CI 0·38–0·47]; p<0·001) than natural immunity up to the first 2 months, with evidence of attenuation thereafter up to 9 months (p<0·001) of follow-up. During a mean follow-up of 66 days (SD 53) in cohort 3, 438 individuals with two-dose hybrid immunity were registered as having had a SARS-CoV-2 reinfection, compared with 808 individuals with natural immunity (numbers of hospitalisations were six and 40, respectively). Two-dose hybrid immunity was associated with a 66% lower risk of SARS-CoV-2 reinfection (aHR 0·34 [95% CI 0·31–0·39]; p<0·001) than natural immunity, with no significant attenuation up to 9 months (p=0·07). To prevent one reinfection in the natural immunity cohort during follow-up, 767 individuals needed to be vaccinated with two doses. Both one-dose (HR adjusted for age and baseline date 0·06 [95% CI 0·03–0·12]; p<0·001) and two-dose (HR adjusted for age and baseline date 0·10 [0·04–0·22]; p<0·001) hybrid immunity were associated with a lower risk of COVID-19 hospitalisation than natural immunity.

Interpretation. The risk of SARS-CoV-2 reinfection and COVID-19 hospitalisation in individuals who have survived and recovered from a previous infection remained low for up to 20 months. Vaccination seemed to further decrease the risk of both outcomes for up to 9 months, although the differences in absolute numbers, especially in hospitalisations, were small. These findings suggest that if passports are used for societal restrictions, they should acknowledge either a previous infection or vaccination as proof of immunity, as opposed to vaccination only.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00143-8/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900143-8/fulltext)

**title:** It is vital that we retain some reliable covid-19 surveillance tools

BMJ| 5th april 2022

*Sylvia Richardson, president*
Like many others, I was alarmed by the news that the REACT programme was discontinued at the end of March. There also remains considerable uncertainty over whether other covid surveillance studies will stay in place and if they do whether they’ll be reduced in size.

Throughout the pandemic, surveillance studies such as REACT and the ONS Covid Infection Survey have provided vital insights into the prevalence of the disease over time. Because they survey a random sample of the population, they provide trustworthy estimates of prevalence which are not influenced by the reasons people get tested. Early on, one of the key discoveries of the pandemic was REACT’s finding that up to a third of infected individuals are still able to spread the disease despite being asymptomatic themselves.1 In the last few weeks, as cases rise again, REACT has found an increase of prevalence in those aged 55 and over, suggesting waning immunity.2

The requirement in England for people testing positive for covid to self-isolate ended in February and restrictions for travel ended last month, so community surveillance studies are now more important than ever. We are entering a new phase of the pandemic where people’s behaviour will change substantially and their immunity may also be changing—it is vital that we retain some reliable surveillance tools.

Over the last two years, along with the contact tracing system, these studies have done a sterling job at detecting new variants at speed so public health decisions could be made quickly to help reduce spread. Without these timely data, we would be missing a crucial element to policy making and putting the public’s health at risk. They are also not only helpful when the disease is at its peak but once set up can be expanded in an agile way to investigate additional health concerns, such as long covid. Relying on self reported tests alone is no way to proceed. These datasets are likely to be biased by selective reporting: some people will not report their negative tests and, now that a PCR is no longer required to confirm a positive LFT, how many will not be reporting their positive tests either? The situation is exacerbated now that free testing for both symptomatic and non-symptomatic cases has ended (as of 1 April 2022), which will both significantly reduce the number of people testing and introduce an additional bias as, presumably, those with more disposable income are more likely to take tests.

The “Living with Covid” plan was announced by the government with great fanfare, but lacks a clear data strategy: what studies and resources does the government intend to keep? How will they track new variants? We need more transparency around this. While the government’s plan puts the focus on the importance of vaccines in curbing the spread, it is surveillance studies that can monitor the effectiveness of these vaccines and waning immunity.

Of course, public funding is not unlimited, especially when the focus on covid spending has meant that other areas have been neglected. But surveillance studies cost little compared to other measures. The annual cost of the ONS surveillance study is £390m and the Zoe Covid study app which has just been scrapped received around £5m in government funding.45 This compares to £13.5bn spent by Test and Trace in its first year and the nearly £9bn that was recently revealed to have been spent on unusable personal protective equipment (PPE). Indeed, ending these studies could prove much costlier in the long run if it means our health systems and economy are taken by surprise by a new wave of the disease linked to more severe variants. If studies are to be scaled down or ended completely this should not be led by arbitrary cost-cutting targets. Statisticians and others who have tirelessly led on this work must be consulted so that damaging discontinuities can be managed. We need to be able to assess whether the government’s new approach to curbing covid is the right one and we can only do this by monitoring basic epidemiological quantities such as prevalence in a reliable way. The health secretary told the public that they should be prepared for cases to rise as restrictions ended but what we have seen is a lack of preparedness from the government on how they will deal with an evolving disease and situation.

The UK has been a world leader in its surveillance of covid, building systems from scratch which have allowed us to track the virus at a speed and scale never seen before. As the pandemic is far from over, now is not the time to undo all this good work.
<https://www.bmj.com/content/377/bmj.o900>

**title:** Disincentives for vaccine refusal

BMJ| 31st march 2022

As the world adjusts to living with covid-19 and its variants such as omicron, the need to boost vaccination rates is paramount. Some countries are attempting to force the hand of people who are less willing to be vaccinated by pivoting from incentives to disincentives.

Perhaps the most major disincentives are vaccine mandates, curbing the ability of anyone unvaccinated to move freely in public spaces or to access public services. But, as with the plethora of rewards for vaccination, it remains to be seen whether these have the desired effect. Some experts have warned that, conversely, the heavy-handedness risks alienating and polarising these pockets of the populace for good.

View infographic: <https://www.bmj.com/content/376/bmj.o865>

**title:** Effectiveness of CoronaVac, ChAdOx1 nCoV-19, BNT162b2, and Ad26.COV2.S among individuals with previous SARS-CoV-2 infection in Brazil: a test-negative, case-control study

the lancet infectious diseases | 31st march 2022

COVID-19 vaccines have proven highly effective among individuals without a previous SARS-CoV-2 infection, but their effectiveness in preventing symptomatic infection and severe outcomes among individuals with previous infection is less clear. We aimed to estimate the effectiveness of four COVID-19 vaccines against symptomatic infection, hospitalisation, and death for individuals with laboratory-confirmed previous SARS-CoV-2 infection.

Methods. Using national COVID-19 notification, hospitalisation, and vaccination datasets from Brazil, we did a test-negative, case-control study to assess the effectiveness of four vaccines (CoronaVac [Sinovac], ChAdOx1 nCoV-19 [AstraZeneca], Ad26.COV2.S [Janssen], and BNT162b2 [Pfizer-BioNtech]) for individuals with laboratory-confirmed previous SARS-CoV-2 infection. We matched cases with RT-PCR positive, symptomatic COVID-19 with up to ten controls with negative RT-PCR tests who presented with symptomatic illnesses, restricting both groups to tests done at least 90 days after an initial infection. We used multivariable conditional logistic regression to compare the odds of test positivity and the odds of hospitalisation or death due to COVID-19, according to vaccination status and time since first or second dose of vaccines.

Findings. Between Feb 24, 2020, and Nov 11, 2021, we identified 213 457 individuals who had a subsequent, symptomatic illness with RT-PCR testing done at least 90 days after their initial SARS-CoV-2 infection and after the vaccination programme started. Among these, 30 910 (14·5%) had a positive RT-PCR test consistent with reinfection, and we matched 22 566 of these cases with 145 055 negative RT-PCR tests from 68 426 individuals as controls. Among individuals with previous SARS-CoV-2 infection, vaccine effectiveness against symptomatic infection 14 or more days from vaccine series completion was 39·4% (95% CI 36·1–42·6) for CoronaVac, 56·0% (51·4–60·2) for ChAdOx1 nCoV-19, 44·0% (31·5–54·2) for Ad26.COV2.S, and 64·8% (54·9–72·4) for BNT162b2. For the two-dose vaccine series (CoronaVac, ChAdOx1 nCoV-19, and BNT162b2), effectiveness against symptomatic infection was significantly greater after the second dose than after the first dose. Effectiveness against hospitalisation or death 14 or more days from vaccine series completion was 81·3% (75·3–85·8) for CoronaVac, 89·9% (83·5–93·8) for ChAdOx1 nCoV-19, 57·7% (−2·6 to 82·5) for Ad26.COV2.S, and 89·7% (54·3–97·7) for BNT162b2.

Interpretation. All four vaccines conferred additional protection against symptomatic infections and severe outcomes among individuals with previous SARS-CoV-2 infection. The provision of a full vaccine series to individuals after recovery from COVID-19 might reduce morbidity and mortality.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00140-2/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900140-2/fulltext)

**title:** Association Between SARS-CoV-2 Viral Load in Wastewater and Reported Cases, Hospitalizations, and Vaccinations in Milan, March 2020 to November 2021 [research letter]

jama | 1st april 2022

Several studies have demonstrated that wastewater surveillance can be used to monitor SARS-CoV-2 incidence.1-3 This surveillance intends to overcome the limitations of traditional surveillance indicators,4 such as the number of positive tests, which depends on test availability and indications, or COVID-19–related hospitalizations, which occur weeks after the spread of SARS-CoV-2 and do not include mild or asymptomatic cases. This study evaluated the association between SARS-CoV-2 load in urban wastewater and surveillance indicators of infection prevalence and severity in Milan, Italy…
…In Milan, high wastewater SARS-CoV-2 loads were found when vaccination coverage was high and traditional surveillance indicators suggested limited SARS-CoV-2 prevalence. This result suggests that there was significant circulating virus in the population during this period, including among vaccinated individuals. The SARS-CoV-2 circulation among vaccinated individuals may create modest evolutionary pressure toward resistance to the host’s immune response, making variants with significant transmission advantages more competitive. The current spread of the Omicron variant supports this theory.

This study is limited by the difficulty in translating SARS-CoV-2 wastewater loads into infection prevalence because the variability of loads is affected by factors that can be controlled only partially.4 Nonetheless, the magnitude of the observed trends supports the value of wastewater surveillance to monitor the spread of SARS-CoV-2. In addition, the study was limited to a single city.

The results suggest that vaccines are effective in protecting against symptomatic and severe disease, but that, with high vaccination rates, standard surveillance metrics may not accurately estimate the spread of SARS-CoV-2. Thus, wastewater surveillance may be important as an early warning of virus circulation. These results strengthen the scientific basis of the recommendations from the Centers for Disease Control and Prevention National Wastewater Surveillance System and European Commission to establish systematic SARS-CoV-2 wastewater surveillance networks.
<https://jamanetwork.com/journals/jama/fullarticle/2790911>

**title:** Screening and vaccination against COVID-19 to minimise school closure: a modelling study

the lancet infectious diseases| 1st april 2022

Background. Schools were closed extensively in 2020–21 to counter SARS-CoV-2 spread, impacting students' education and wellbeing. With highly contagious variants expanding in Europe, safe options to maintain schools open are urgently needed. By estimating school-specific transmissibility, our study evaluates costs and benefits of different protocols for SARS-CoV-2 control at school.

Methods. We developed an agent-based model of SARS-CoV-2 transmission in schools. We used empirical contact data in a primary and a secondary school and data from pilot screenings in 683 schools during the alpha variant (B.1.1.7) wave in March–June, 2021, in France. We fitted the model to observed school prevalence to estimate the school-specific effective reproductive number for the alpha (Ralpha) and delta (B.1.617.2; Rdelta) variants and performed a cost–benefit analysis examining different intervention protocols.

Findings. We estimated Ralpha to be 1·40 (95% CI 1·35–1·45) in the primary school and 1·46 (1·41–1·51) in the secondary school during the spring wave, higher than the time-varying reproductive number estimated from community surveillance. Considering the delta variant and vaccination coverage in Europe as of mid-September, 2021, we estimated Rdelta to be 1·66 (1·60–1·71) in primary schools and 1·10 (1·06–1·14) in secondary schools. Under these conditions, weekly testing of 75% of unvaccinated students (PCR tests on saliva samples in primary schools and lateral flow tests in secondary schools), in addition to symptom-based testing, would reduce cases by 34% (95% CI 32–36) in primary schools and 36% (35–39) in secondary schools compared with symptom-based testing alone. Insufficient adherence was recorded in pilot screening (median ≤53%). Regular testing would also reduce student-days lost up to 80% compared with reactive class closures. Moderate vaccination coverage in students would still benefit from regular testing for additional control—ie, weekly testing 75% of unvaccinated students would reduce cases compared with symptom-based testing only, by 23% in primary schools when 50% of children are vaccinated.

Interpretation. The COVID-19 pandemic will probably continue to pose a risk to the safe and normal functioning of schools. Extending vaccination coverage in students, complemented by regular testing with good adherence, are essential steps to keep schools open when highly transmissible variants are circulating.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00138-4/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900138-4/fulltext)

**title:** Modelling results on the impact of COVID-19 testing in schools

the lancet infectious diseases | 1st april 2022

The COVID-19 pandemic has had widespread health, wellbeing, and economic impacts, both from the disease itself and from the measures put in place to try to control it. By mid-April, 2020, school closures had impacted 94% of the world's students, with the duration and impact of closures varying substantially by country.1

As new variants rise and fall, it is vital to understand ways to minimise both educational and social disruption by keeping schools open while also reducing the spread of infection. In The Lancet Infectious Diseases, Elisabetta Colosi and colleagues report modelling results investigating the impact of different potential testing strategies in French primary (ages 6–11 years) and secondary (in this study comprising ages 17–18 years) schools. The results are informed by pre-pandemic data on contact patterns, collected via radio frequency identification tags (wearable sensors that detect proximity), and infection data from pilot screening trials in French primary and secondary schools. Colosi and colleagues use the infection data to estimate the effective reproductive number in schools during the alpha (B.1.1.7) and delta (B.1.617.2) variant waves, informing transmission in an individual-based model of infections that is structured according to the contact pattern data. They conclude that weekly asymptomatic testing could reduce both infections and the number of missed days of school due to reactive class closures.

How do these results compare with other models of school-based testing for COVID-19? Previous work examining SARS-CoV-2 transmission among school pupils in the USA, Canada, and the UK found that asymptomatic testing can reduce school transmission. Similar results from a range of independent studies in different countries at different times can give some confidence of a sound conclusion. However, it is very difficult to quantify a reduction in transmission accurately and robustly. Comparisons between studies are further complicated by the implementation of different potential strategies. In addition, schools in different countries might be sufficiently different in setup that implemented measures might be reasonably expected to have different outcomes.

One aspect that reduces our ability to make robust quantifications in this area is the lack of comprehensive data to inform modelling. A strength of the study by Colosi and colleagues is their use of detailed data on school contact patterns, which allowed representative networks to be built using a data-driven basis. These data are one of the best sources of school contact patterns used in this type of study, and yet they still have inevitable drawbacks as they are, by necessity, from studies of particular schools and they represent pre-pandemic contact patterns. Another attempt to inform contact patterns has been made by Woodhouse and colleagues, who used structured expert judgement to construct their random contact networks. By contrast with the detailed contact pattern data available to Colosi and colleagues, Woodhouse and colleagues' data on school infections were sadly quite sparse (as they rightly acknowledge in the paper) as the data originated from a pilot study and were limited in fitting to the increasing phase of the epidemic. Modelling of SARS-CoV-2 transmission in UK schools has an advantage here, with long-term data available on student and staff absences, as well as reported testing in the relevant age groups. These data have been used by my group (Leng and colleagues ) and by Woodhouse and colleagues to parameterise and validate school-based models. Both groups agree with Colosi and colleagues that testing could have an important effect in reducing infections and school days missed.

In time, as more data become available in a wider range of circumstances, and modelling and analysis of existing data are published, a consensus might be reached on the magnitude of the likely effect of SARS-CoV-2 testing strategies in schools. The work by Colosi and colleagues underscores the value of detailed epidemiological and social data obtained in similar populations to better inform future epidemic control policies.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00163-3/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900163-3/fulltext)

**title:** Association of COVID-19 Vaccination During Early Pregnancy With Risk of Congenital Fetal Anomalies

jama pediatrics| 4th april 2022

Pregnant individuals with SARS-CoV-2 infection experience increased maternal and neonatal morbidity.1-3 Although effective COVID-19 vaccines became available in December 2020, pregnant people were excluded from initial trials. Whereas data suggest that COVID-19 vaccines are safe and effective during pregnancy, there is concern about whether the vaccines are associated with risks to the fetus.4 We evaluated the association between COVID-19 vaccination during early pregnancy and risk of major fetal structural anomalies identified on ultrasonography.

Methods. This cohort study included pregnant people receiving care at a quaternary medical center in Chicago, Illinois, who completed a fetal anatomic survey between March and November 2021 and had COVID-19 vaccination records. This study followed the STROBE reporting guideline. The Northwestern University institutional review board provided approval, with a waiver of informed consent because data were collected retrospectively and each participant could not be contacted. Most pregnant people who delivered neonates at the center received outpatient care in community practices. Patient characteristics were abstracted from electronic medical records (EMRs). Race and ethnicity were self-reported and were included to assess whether vaccination uptake varied among racial and ethnic groups. First vaccination date was obtained from EMRs and the Illinois Comprehensive Automated Immunization Registry Exchange and included both messenger RNA and adenovirus vector vaccines. Thirty days before conception until 14 weeks’ gestation was considered the teratogenic window. Participants were considered unvaccinated if there was EMR documentation of declination of vaccination. Fetal congenital anomalies were defined as structural anomalies identifiable in the second trimester (eg, 18-24 weeks’ gestation) that may affect a neonate’s life expectancy, health, or functioning and were categorized according to the Brighton Collaboration Congenital Anomalies Working Group recommendations.5 Functional defects (eg, galactosemia) cannot be assessed using ultrasonography and thus were excluded. Sonographic interpretation was performed by perinatologists or obstetrics and gynecology specialists with additional training in obstetric ultrasonography. Vaccination status was not routinely available to clinicians at the time of ultrasonography.

Primary analyses compared unvaccinated individuals and those vaccinated outside the teratogenic window (ie, individuals without a potential teratogenic exposure) with those vaccinated within the teratogenic window. Analyses were conducted using Stata, version 15.0. Sensitivity analyses used a narrower teratogenic window to categorize exposure (2-10 weeks’ gestation). Two-sided P < .05 was considered significant.

Results. Of 3156 patients (100% female; mean [SD] age, 33.4 [4.6] years) who met the inclusion criteria, 2622 (83.1%) received at least 1 vaccine dose and 1149 (43.8%) were vaccinated within the teratogenic window (Table 1). An anomaly was identified in 27 of 534 unvaccinated people (5.1%) and 109 of 2622 people who received at least 1 dose of vaccine (4.2%) (P = .35). Similar findings were seen when the teratogenic window was narrowed (Table 2). After controlling for potential confounders (age at delivery, nulliparity, chronic hypertension, and hemoglobin A1c level during the first trimester), vaccination within the teratogenic window was not associated with presence of a congenital anomaly identified on ultrasonography (adjusted odds ratio, 1.05; 95% CI, 0.72-1.54).

Discussion. In 3% to 5% of births in the US, neonates are born with structural defects, which are associated with increased infant morbidity, mortality, and billions of dollars in cost.5,6 Our findings suggest that COVID-19 vaccination during early pregnancy is not associated with an increased risk of fetal structural anomalies identified with ultrasonography.

The findings are limited by the retrospective, single-center origin of the data and by limitations of EMRs. Not all confounding variables could be reasonably ascertained (eg, folic acid intake). Furthermore, ultrasonography markers are surrogate outcomes, and many pregnancies in the data set are ongoing; thus, neonatal outcomes were not uniformly available. Given the urgent need for safety data on COVID-19 vaccines, these preliminary findings may be useful when considering vaccination during early pregnancy. The adjustment for preexisting risk factors (eg, hyperglycemia) allowed for a better understanding of associations between vaccination and anomalies. Clinicians may use this evidence in counseling their patients on the safety of vaccination.
<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2790805>

**title:** Impact of donor vaccination on recipient response to early SARS-CoV-2 mRNA vaccination after allogeneic HSCT

THE LANCET haematology| 1st april 2022

The first two oral antivirals, molnupiravir and nirmatrelvir–ritonavir, are now becoming available in
Since the emergence of COVID-19 more than 2 years ago, allogeneic haematopoietic stem-cell transplantation (HSCT) recipients have been considered at especially high risk of developing severe forms of the disease. The first studies focusing on COVID-19 after HSCT confirmed the poor prognosis in this population, highlighting the urgent need for efficient preventive and curative treatment strategies. In this regard, mRNA vaccines have emerged with the ability to confer a high protection rate, mostly against severe disease, and a good safety profile; however, in post-HSCT vaccination, humoral response might be altered due to intake of immunosuppressive drugs and delay of B-cell recovery. Although a weak immune response after two doses of mRNA vaccine against SARS-CoV-2 has been reported in around 40% of allogeneic HSCT recipients, a third early vaccine dose has been shown to have a positive impact on humoral response in this subpopulation of poorly responding recipients. We addressed whether pre-HSCT vaccination of donors has an impact on humoral response to early post-HSCT vaccination of recipients, at a time when they are still receiving immunosuppressive drugs…

…In conclusion, our study suggests that pre-HSCT donor vaccination has an impact on post-HSCT humoral response to early SARS-CoV-2 mRNA vaccination after HSCT. Although these results require further validation, they provide a rationale for incorporating donor serological status against SARS-CoV-2 into the algorithm of donor choice, or inciting donor vaccination before donation, if feasible. We believe that early and efficient vaccination of every HSCT recipient should be a priority, starting at 3 months post-HSCT. The number of required initial doses should be determined by careful monitoring of humoral response, with the possibility of a booster dose 6 months later. During the early months after HSCT, while awaiting an efficient anti-SARS-CoV-2 immune response to be attained, treatment options like pre-exposure and post-exposure prophylaxis with neutralising monoclonal antibodies could be considered.
[https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(22)00097-7/fulltext](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026%2822%2900097-7/fulltext)

**title:** Methotrexate and TNF inhibitors affect long-term immunogenicity to COVID-19 vaccination in patients with immune-mediated inflammatory disease

THE LANCET rheumatology| 1st april 2022

Since the emergence of the COVID-19 pandemic, confirmed cases and cumulative deaths have been
…Although the relevance of our findings are constrained by the small sample size and scarcity of established correlates of levels of immunogenicity to efficacy, they show that both methotrexate and TNF inhibitors might lead to a dampened humoral response to COVID-19 vaccinations. Although TNF inhibitors do not demonstrate an initial effect on immunogenicity, persistence of adequate humoral response is significantly decreased by month 6 (appendix p 11). Taken together, these findings support the use of supplemental booster dosing in patients with immune-mediated inflammatory diseases, and specifically for those being treated with TNF inhibitors or TNF inhibitor–methotrexate combination therapy. Larger studies are needed to validate these results and to assess the effects of other immunomodulatory therapies, which will help to identify optimal timing and strategy of COVID-19 (and potentially other) vaccines.
[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00069-8/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913%2822%2900069-8/fulltext)

**title:** Covid-19: WHO suspends supplies of India’s Covaxin through UN agencies

bmj| 6th april 2022

The World Health Organization has suspended the supply of Covaxin through UN procurement agencies because of manufacturing irregularities. Covaxin is India’s indigenous covid-19 vaccine, produced by the Hyderabad based Bharat Biotech. A spokesperson for WHO told The BMJ that the suspension had come after a broader inspection of a few companies in India by the agency…
<https://www.bmj.com/content/377/bmj.o902>

**title:** Dynamics of humoral and T-cell immunity after three BNT162b2 vaccinations in adults older than 80 years

the lancet infectious diseases| 6th april 2022

…We conclude that a third dose of BNT162b2 in older adults, while establishing immunity in primary non-responders,4 induces a durably escalated humoral response in the bulk of vaccinees for at least 3 months, indicating longer lasting humoral immunity. In a younger cohort, this boost also led to a strong increase of neutralising antibodies against the omicron (B.1.1.529) variant and protection from infection with the omicron variant.5, 6 Although neutralising antibody data for omicron are not yet available for our cohort, the strong rise in titres of neutralising antibodies against the BavPat1/2020 isolate used in our neutralisation assay (appendix p 5) suggests better neutralisation against omicron by the booster dose than for the second dose, as also demonstrated by others,7 at least in the short term. The level of T-cell immunity to SARS-CoV-2 in peripheral blood required for protection is still not established, although peripheral T cells induced by BNT162b2 apparently react well against the omicron variant.8 As for our cohort, our data show two important aspects of a third compared with a second dose—namely, peak virus-specific T-cell frequencies were not further increased by a third dose, and average per-cell production of IFNγ remained unaltered and was still remarkably lower than in recovered donors of a similar age. Thus, at least in older adults, the durability and quality of vaccine-induced immunity should be considered in the recommendation of booster vaccinations, in addition to the severity of breakthrough SARS-CoV-2 infections caused by current and future viral mutants.
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00219-5/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900219-5/fulltext)

**title:** Determinants of uptake of a third dose of SARS-CoV-2 vaccines in patients with inflammatory bowel disease

the lancet gastroenterology & hepatology | 6th april 2022

…Patients with inflammatory bowel disease (IBD) are frequently treated with immunosuppressive treatments that can affect serological responses to SARS-CoV-2 vaccination.1 On Sept 1, 2021, the Joint Committee on Vaccination and Immunisation recommended a third dose for immunosuppressed patients, with patients with IBD eligible after Nov 26, 2021.2

We assessed SARS-CoV-2 third dose vaccination uptake in patients with IBD receiving infliximab or vedolizumab infusions at John Radcliffe Hospital (Oxford, UK) and the Royal London Hospital (London, UK). All patients were initially recruited in April, 2020, for our ongoing SARS-CoV-2 seroprevalence study and included if still attending the infusion units at the time of data collection (459 patients in Oxford, and 295 patients in London).3 21 patients could not be contacted (mainly because they changed addresses or hospitals) or switched therapies. These were all patients in London, which might reflect a difference in demographic factors (eg, moving houses more often) and the greater tendency at the London centre to offer subcutaneous treatments as an alternative to infusions. Thus, 733 patients were included in our analysis. Vaccination status was determined via electronic medical records (Electronic Patient Records and the National Immunisation and Vaccination System) on March 2, 2022…

…In conclusion, although the uptake of the third dose of SARS-CoV-2 vaccination in patients with IBD attending infusion centres in Oxford and London is higher than the national uptake, younger patients, patients with Crohn's disease, patients of non-White ethnicity, and of lower socioeconomic status show higher rates of vaccine hesitancy. Given the evidence that a third dose of vaccine is critical to confer adequate protection against the dominant omicron variant,5 addressing this issue in this vulnerable patient population is of utmost clinical importance.
[https://www.thelancet.com/journals/langas/article/PIIS2468-1253(22)00120-0/fulltext](https://www.thelancet.com/journals/langas/article/PIIS2468-1253%2822%2900120-0/fulltext)

**title:** Protection with a Third Dose of mRNA Vaccine against SARS-CoV-2 Variants in Frontline Workers

new england journal of medicine | 6th april 2022

Data are needed regarding the effectiveness of a third dose of a messenger RNA (mRNA) vaccine against the B.1.1.529 (omicron) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that are based on scientifically rigorous, population-level surveillance. Health care personnel, first responders, and other essential and frontline workers who are being evaluated in the HEROES-RECOVER cohorts at eight sites in six states across the United States underwent weekly reverse-transcriptase–polymerase-chain-reaction (RT-PCR) testing regardless of the presence or absence of coronavirus disease 2019 (Covid-19) symptoms.1-3 Here, we report the vaccine effectiveness of two or three doses of an mRNA vaccine against infection caused by the omicron and B.1.617.2 (delta) variants…

… In this prospective cohort of frontline workers, a third mRNA vaccine dose provided strong (91%) protection against delta infection, similar to the findings of a study showing an effectiveness of 89 to 94% for three doses of mRNA vaccine against medically attended Covid-19 during a period when the delta variant was predominant.4 In contrast, our estimate of vaccine effectiveness of 60% for three doses against omicron infection was lower than the corresponding effectiveness of three doses against medically attended Covid-19 (82 to 90%) in the same study. Although in our study a third dose improved protection against omicron infection (relative vaccine effectiveness, 60%), relative protection was much higher against delta infection (86%). Lower vaccine effectiveness against mild or asymptomatic omicron infection is consistent with recent data showing lower protection in the ambulatory care setting and among adults who were tested for SARS-CoV-2 during the periods of circulation of the delta and omicron variants.5 Despite indicating a decline in vaccine effectiveness, these results show continued effectiveness against clinically severe outcomes related to both variants.
<https://www.nejm.org/doi/full/10.1056/NEJMc2201821?query=featured_coronavirus>

**title:** Protection by a Fourth Dose of BNT162b2 against Omicron in Israel

new england journal of medicne | 5th april 2022

On January 2, 2022, Israel began administering a fourth dose of BNT162b2 vaccine to persons 60 years of age or older. Data are needed regarding the effect of the fourth dose on rates of confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and of severe coronavirus disease 2019 (Covid-19)…

METHODS. Using the Israeli Ministry of Health database, we extracted data on 1,252,331 persons who were 60 years of age or older and eligible for the fourth dose during a period in which the B.1.1.529 (omicron) variant of SARS-CoV-2 was predominant (January 10 through March 2, 2022). We estimated the rate of confirmed infection and severe Covid-19 as a function of time starting at 8 days after receipt of a fourth dose (four-dose groups) as compared with that among persons who had received only three doses (three-dose group) and among persons who had received a fourth dose 3 to 7 days earlier (internal control group). For the estimation of rates, we used quasi-Poisson regression with adjustment for age, sex, demographic group, and calendar day…

… CONCLUSIONS

Rates of confirmed SARS-CoV-2 infection and severe Covid-19 were lower after a fourth dose of BNT162b2 vaccine than after only three doses. Protection against confirmed infection appeared short-lived, whereas protection against severe illness did not wane during the study period.
<https://www.nejm.org/doi/full/10.1056/NEJMoa2201570?query=featured_coronavirus>

**title:** Maternal COVID-19 Vaccine Safe for Infants

jama | 5th april 2022

A study in Israel found that individuals who received an mRNA COVID-19 vaccine during pregnancy delivered infants with no increased risk for morbidity or mortality compared with infants whose birthing parents weren’t vaccinated.

The investigators analyzed 24 288 singleton live births from a health care organization in Israel from March 2021 through September 2021. The study included 16 697 newborns exposed in the first and second trimesters to maternal vaccination with the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech)…
<https://jamanetwork.com/journals/jama/article-abstract/2790650>

**title:** Assessment of Provision of COVID-19 Vaccination in Dialysis Clinics and Patient Vaccination Coverage

jama internal medicine| 4th april 2022

For patients who undergo maintenance dialysis, COVID-19 is associated with increased risk for severe illness and death.1-3 However, this population was not specifically recommended to be prioritized for COVID-19 vaccination.4 On March 25, 2021, a federal effort was announced to offer COVID-19 vaccinations in dialysis clinics as part of the COVID-19 Health Equity Plan.5 Two national dialysis care organizations—DaVita Inc and Fresenius Medical Care—partnered with the Centers for Disease Control and Prevention (CDC) to provide COVID-19 vaccination in their clinics and coordinate vaccine distribution to other dialysis organizations. We evaluated COVID-19 vaccination in dialysis clinics, vaccination coverage, and disparities from December 1, 2020, to June 13, 2021…
<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2790866>

**HEALTH MANGEMENT**

**title:** Managing Healthcare Staff With Symptoms Of A Respiratory Infection Or A Positive Covid-19 Test Result

UK HEALTH SECURITY AGENCY | 1st april 2022

This guidance is for staff and managers in health care settings and includes guidance for patient-facing health care staff if they develop symptoms of a respiratory infection including coronavirus (Covid-19), receive a positive Covid-19 test result, or are a contact of a confirmed case of Covid-19.
<https://kingsfund.blogs.com/health_management/2022/04/managing-healthcare-staff-with-symptoms-of-a-respiratory-infection-or-a-positive-covid-19-test-resul.html>

**recovery**

**title:** Pandemic saw large rise in patients self-funding hip and knee replacements

bmj | 31st march 2022

The number of UK patients self-funding their own hip and knee operations has risen substantially since the start of the covid pandemic, new figures show. Data from the Private Healthcare Information Network1 show that 4732 people self-funded hip replacements from July to September 2021, up by 164% from 1795 in the same period in 2019. The same periods saw a 119% rise in people self-funding knee replacements, up from 1117 to 2448, as well as a 64% rise in those paying out of their pockets for cataract operations, up from 8091 to 13 231. Throughout those periods the data showed a 16% drop in people paying for private healthcare through their own insurance policy, down from 141 900 to 119 100. Matt James, chief executive of the Private Healthcare Information Network, said, “Our data shows a significant rise in people paying out of their own pocket for common procedures like joint replacements and cataract surgery since the pandemic. However, levels of private care overall are flat, as activity levels for people who have private insurance remain lower after the pandemic.”

In the three months from July to September 2019, 49 700 people opted to self-fund all types of private treatment. In the corresponding months in 2021, 67 100 people chose this route, a 35% rise. In contrast, patients paying through pre-existing insurance policies showed only single digit percentage rises during these periods.

The figures also show that consultants are moving back to work in the private sector after a period of being focused on supporting the NHS during the pandemic, but there are still fewer consultants actively treating private patients than before the pandemic.

In April 2020, 1800 consultants were actively providing private healthcare. This figure has risen to 8100 as of September 2021 but is still short of pre-pandemic levels, when as many as 9200 consultants were actively providing private care in September 2019.
<https://www.bmj.com/content/376/bmj.o822.full>

**title:** Validation of Home Visual Acuity Tests for Telehealth in the COVID-19 Era

jama opthalmology | 31st march 2022

Question Are at-home tests valid for measurement of visual acuity during the COVID-19 pandemic?

Findings In this randomized, comparative effectiveness research study, at-home acuity tests were performed by participants in their own homes and results were compared with standard-of-care visual acuity measurements during a clinic visit. Compared with in-office acuity measurements, all 3 at-home tests were within 1 line of Snellen acuity.

Meaning In this study, 3 at-home visual acuity tests were validated through comparison with in-office visual acuity measurements, supporting their potential use in teleophthalmology care.
<https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2790590>

**title:** Association Between Primary Care Practice Telehealth Use and Acute Care Visits for Ambulatory Care–Sensitive Conditions During COVID-19

national audit office | 30th march 2022

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

**title:** Association Between Primary Care Practice Telehealth Use and Acute Care Visits for Ambulatory Care–Sensitive Conditions During COVID-19

jama| 31st march 2022

Question What is the association between a primary care practice’s degree of telehealth use and acute care visits for ambulatory care–sensitive conditions during the COVID-19 pandemic?

Findings In this cohort study with a difference-in-differences analysis of insurance claims data from 4038 primary care practices, high primary care telehealth use was associated with 2.10 more emergency department visits or hospitalizations for ambulatory care–sensitive conditions per 1000 patients per year compared with the practices with the least telehealth use.

Meaning These findings suggest that high levels of primary care practice telehealth use may result in slightly higher acute care visits for ambulatory care–sensitive conditions.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790571>

**title:** Use of Telehealth Across Pediatric Subspecialties Before and During the COVID-19 Pandemic

the lancet | 2nd april 2022

Question How has telehealth use during the COVID-19 pandemic varied across pediatric subspecialties, and was telehealth associated with changes in no-show rates and access disparities?

Findings This cohort study of 8 large pediatric medical groups in California found high variability in telehealth use across subspecialties but no association between telehealth volume and clinic no-show rates. Although overall visits remained stable from the prepandemic to pandemic periods, English-speaking patients and patients of ethnicities other than Hispanic were more likely to be seen via telehealth.

Meaning Documenting variation in telehealth adoption can inform telehealth policy, including the appropriateness of telehealth for different patient needs and areas where additional tools are needed to promote use.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790578>

**title:** Helen Salisbury: Open doors and open windows

BMJ| 5th april 2022

One in 10 Americans say that their religious beliefs prohibit them from getting covid-19 vaccines,1
Our practice has finally reverted to its pre-pandemic appointment system. Patients can book by telephone, online, or in person for either a face-to-face or a telephone appointment, according to what they think they need. They can also submit e-consultation forms. When we had to use telephone triage for all appointments earlier in the pandemic it reduced our efficiency: if, after a five minute conversation with a patient, you decided that you couldn’t safely manage them or sort out their problem without an examination, another appointment was needed.

The conversion rate of telephone to face-to-face appointments varied between clinicians, but we all shared a sense of work being postponed or incomplete. We’d try to book face-to-face follow-ups with the same doctor, but this wasn’t always possible in a suitable timeframe, so a second clinician had to pick up where the first one left off. In this situation you can either take the history again from scratch (which is inefficient) or rely on what your colleague has written, which will inevitably leave out some of the nuances around what was said. This loss of continuity isn’t just about information—it also affects rapport, which you need to establish afresh if you take over midway.

In theory, a written e-consultation might take the place of the original phone appointment, but in practice this often just turns a two stage process into a three stage one, with a form to read, a phone call to clarify, and a face-to-face appointment to examine.

We’re not completely back to normal. We’re still wearing scrubs—not because there’s any evidence of fomite transmission of SARS-CoV-2 but as a visual reminder to our patients that the pandemic’s not over. We wear FFP2 masks for all patient contacts, and we expect our patients to wear masks too. We also open the windows wide after each consultation, to change the air. Very occasionally, patients decline to wear masks, in which case my window stays open throughout. This was fine during the brief spell of warm weather in mid-March and less fun when snow was blowing in over my desk last week, but, given that I was doing an extra surgery to cover for a colleague absent with covid, I was in no mood to compromise. It’s still early days for our “new normal,” and we don’t yet know how well it will work, although we expect that more patients than before will choose the telephone for simple, transactional appointments. However, we’re also aware that although no physical examination may be needed, some people find that being in the same room as the doctor contributes significantly to feeling heard and understood. As a doctor who is trained to use all of my senses and not just my ears, this is less stressful for me, and I’m more confident when I can see, touch—and occasionally even smell—my patients.
<https://www.bmj.com/content/377/bmj.o883>

**public health**

**title:** Mental Health Service Use, Suicide Behavior, and Emergency Department Visits Among Rural US Veterans Who Received Video-Enabled Tablets During the COVID-19 Pandemic

jama | 6th april 2022

Question Was the US Veterans Affairs initiative to distribute video-enabled tablets during COVID-19 associated with mental health care access, suicide behavior, or emergency department (ED) visits among rural veterans?

Findings In this retrospective cohort study of 471 791 rural US veterans with a history of mental health care use, receipt of a video-enabled tablet was associated with increased use of mental health care via video, increased psychotherapy visits (across all modalities), and reduced suicide behavior and ED visits.

Meaning These findings suggest that video-enabled tablets may provide access to critical services for rural patients with mental health needs and reduce instances of suicide behavior and ED visits among them.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790743>

**international perspectives**

**title:** Rwanda’s success in rolling out its covid-19 vaccination campaign is a lesson to us all

bmj | 1st april 2022

The discovery and approval of effective and safe covid-19 vaccines has provided a glimmer of hope during a seemingly intractable crisis. The vaccines were rapidly distributed across the globe, with priority given to the most at-risk populations in many rich countries.1 While many have called for the equitable distribution of vaccines across the globe through COVAX, and continue to do so, this continues to be far from the reality. As of 1 April 2022, 64.5% of the world’s population has received at least one dose of the vaccine; yet, this proportion is only 14.5% in low-income countries.2 It is in this context of vast vaccine inequity that we discuss Rwanda’s vaccination strategy and milestones over the past year…
<https://www.bmj.com/content/377/bmj.o881>

**title:** Projecting COVID-19 Mortality as States Relax Nonpharmacologic Interventions

JAMA | 1st april 2022

COVID-19 has amplified inequalities in global health and socioeconomic outcomes between HICs and
Question What is the expected trend in COVID-19 mortality if US states were to lift nonpharmacologic interventions (NPIs) at different times over the remainder of 2022?

Findings In this simulation modeling study, lifting NPIs was likely to result in rebounding epidemics regardless of the delay in lifting. The degree of population-level immunity was associated with the size of the rebounding peak in incident deaths.

Meaning This simulation study found no path to the end of the COVID-19 pandemic that avoided difficult trade-offs between prolonged NPIs and increased COVID-19 mortality following their removal.
<https://jamanetwork.com/journals/jama-health-forum/fullarticle/2790812>

**title:** Not Ready for the End Game — Why Ending Federal Covid-19 Emergency Declarations Will Harm Access to Care

new england journal of medicine | 6th april 2022

COVID-19 has amplified inequalities in global health and socioeconomic outcomes between HICs and
Increasing demands that President Joe Biden “end the emergency” reflect political symbolism and understandable longing for normal life. But responding literally, by abruptly terminating federal emergency declarations, will backfire. Doing so will not eliminate the mask, vaccination, and quarantine requirements some Americans oppose — many of which are being discontinued anyway. Moreover, rushed terminations of federal emergency declarations will eliminate regulatory flexibility and financial supports for patients, providers, and the health care system…
<https://www.nejm.org/doi/full/10.1056/NEJMp2203468>

**title:** Vaccine Uptake in the US After Full Food and Drug Administration Approval of the BNT162b2 mRNA COVID-19 Vaccine

JAMA | 6th april 2022

On August 23, 2021, the US Food and Drug Administration (FDA) gave its first full approval of a COVID-19 vaccine, the BNT162b2 mRNA vaccine (Pfizer-BioNTech).1 Previously, a Kaiser Family Foundation survey2 found that many unvaccinated individuals were concerned the vaccine was unsafe, and some remained unvaccinated because they did not trust the government. It is unclear whether FDA approval allayed this hesitancy. To examine this notion, we conducted a cross-sectional analysis of the association between the FDA full approval of BNT162b2 mRNA vaccine with subsequent US COVID-19 vaccinations of any kind.

…To our knowledge, this cross-sectional study is the first to examine the association of the FDA’s full approval of the BNT162b2 mRNA COVID-19 vaccine with subsequent US COVID-19 vaccinations. We estimated that approval was significantly associated with an increase in the overall number of vaccines administered; however, this appears to be largely related to an increase in series completions after approval. Our analysis suggests that approval may have been associated with a decrease in the number of first doses administered compared with what would have been expected without approval. Potential limitations of this study include the possibility of spillover effects and the relative shortness of the postintervention period considered.

Additional research is needed to understand the underlying reasons for this differential response to FDA approval. Individuals who have not received any dose of a COVID-19 vaccine may be behaviorally distinct from those who have chosen to receive at least 1 dose. The results in the unvaccinated population may be related to negative perceptions of government sources of vaccine information. Alternatively, some may have decided to postpone taking vaccines from other manufacturers to reevaluate their vaccine choices considering approval of the Pfizer-BioNTech vaccine. The contrasting relative increase of series completions may reflect that approval was associated with the decisions of individuals who forgot or had barriers to scheduling a second appointment or previously had misgivings after taking the first dose.

Our results call for more research into the association of FDA approval with US vaccine uptake. They also call for more work into the distinctions between unvaccinated individuals and those who have received 1 dose to improve our understanding of how interventions could motivate the 2 groups toward full vaccination.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790748>

**title:** At-home COVID-19 Test Instructions Frequently Misinterpreted

jama| 5th april 2022

The US Food and Drug Administration (FDA) instructions accompanying at-home SARS-CoV-2 rapid self-tests often confused people in a recent trial reported in JAMA Internal Medicine, causing them to incorrectly decide not to quarantine.

The 360 adults in the study participated in an online survey that assessed how they would interpret the results of a home test. Participants were randomly assigned to receive 1 of 3 different instructions: the FDA-authorized instructions, the intervention instructions, or no instructions. Decision science principles—including using simple wording and clearly describing different scenarios’ implications—guided the intervention instructions’ design…
<https://jamanetwork.com/journals/jama/article-abstract/2790651>

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