COVID-19 weekly update

14th April 2022

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| [Clinical management](#Clinical)  [Rates & variants](#Rates)  [Infection control](#Infection) | [Workforce well-being](#Workforce)  [Health management & recovery](#Management) | [Public health & health inequalities](#Public) [International perpsectives](#International) |

**clinical management**

**title:** Covid-19: What is the evidence for the antiviral molnupiravir?

bmj| 13th april 2022  
  
Merck’s drug was originally claimed to halve hospital admissions and deaths in people with covid-19, leading some governments to stockpile it as the pandemic continued. Andy Extance looks at the published evidence for its effectiveness.

What is molnupiravir? Molnupiravir (marketed as Lagevrio) is an antiviral drug, slightly modified from a compound known as NHC (β-d-N4-hydroxycytidine) that a team at Emory University in Atlanta, Georgia, first described in 2003.1 It is available as hard capsules that are swallowed and adsorbed from the gut so is easy to take at home. That contrasts with some other covid-19 drugs such as the monoclonal antibody tocilizumab or the antiviral remdesivir, which must be administered by intravenous infusion in hospitals. In October 2021 the UK government announced the procurement of 480 000 courses of molnupiravir (as well as 250 000 courses of the Pfizer antiviral Paxlovid (nirmatrelvir)).

Molnupiravir had been due to enter clinical trials against influenza, but during the pandemic Emory University struck a deal with the biotechnology company Ridgeback Biotherapeutics to test it as a treatment for covid-19.2 Ridgeback then partnered with the pharmaceutical giant Merck in May 2020 for clinical trials and scale-up.

Antiviral drugs for acute respiratory infections need to be used as early as possible after infection if they are to help prevent disease progression, hospital admissions, and deaths. This normally means within three days, but the drug may still be beneficial up to five days after onset of symptoms. The current advice is to give 800 mg of molnupiravir (four 200 mg tablets) every 12 hours for five days, within five days of symptom onset…  
<https://www.bmj.com/content/377/bmj.o926>

**title:** Inhaled corticosteroids: not just for asthma, but for COVID-19?

JAMA network open| 12th april 2022  
  
Question. Is subcutaneous treatment with casirivimab and imdevimab associated with improved 28-day clinical outcomes compared with nontreatment, and is it clinically similar to intravenously administered casirivimab and imdevimab for outpatients with COVID-19?

Findings. In this cohort study of 1959 propensity-matched outpatients with mild to moderate COVID-19 symptoms, the 28-day rate of hospitalization or death was 3.4% vs 7.0% for those receiving subcutaneous treatment vs nontreatment. In a second cohort analysis of 2185 outpatients, the 28-day rate of hospitalization or death was 2.8% vs 1.7% for subcutaneous vs intravenous treatment.

Meaning. Subcutaneous casirivimab and imdevimab was associated with reduced hospitalization and death compared with nontreatment and showed similar outcomes compared with intravenous casirivimab and imdevimab in outpatients with COVID-19.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790990>

**title:** Early Th2 inflammation in the upper respiratory mucosa as a predictor of severe COVID-19 and modulation by early treatment with inhaled corticosteroids: a mechanistic analysis

the lancet respiratory medicine| 7th april 2022  
  
Background. Community-based clinical trials of the inhaled corticosteroid budesonide in early COVID-19 have shown improved patient outcomes. We aimed to understand the inflammatory mechanism of budesonide in the treatment of early COVID-19.

Methods. The STOIC trial was a randomised, open label, parallel group, phase 2 clinical intervention trial where patients were randomly assigned (1:1) to receive usual care (as needed antipyretics were only available treatment) or inhaled budesonide at a dose of 800 μg twice a day plus usual care. For this experimental analysis, we investigated the nasal mucosal inflammatory response in patients recruited to the STOIC trial and in a cohort of SARS-CoV-2-negative healthy controls, recruited from a long-term observational data collection study at the University of Oxford. In patients with SARS-CoV-2 who entered the STOIC study, nasal epithelial lining fluid was sampled at day of randomisation (day 0) and at day 14 following randomisation, blood samples were also collected at day 28 after randomisation. Nasal epithelial lining fluid and blood samples were collected from the SARS-CoV-2 negative control cohort. Inflammatory mediators in the nasal epithelial lining fluid and blood were assessed for a range of viral response proteins, and innate and adaptive response markers using Meso Scale Discovery enzyme linked immunoassay panels. These samples were used to investigate the evolution of inflammation in the early COVID-19 disease course and assess the effect of budesonide on inflammation.

Findings. 146 participants were recruited in the STOIC trial (n=73 in the usual care group; n=73 in the budesonide group). 140 nasal mucosal samples were available at day 0 (randomisation) and 122 samples at day 14. At day 28, whole blood was collected from 123 participants (62 in the budesonide group and 61 in the usual care group). 20 blood or nasal samples were collected from healthy controls. In early COVID-19 disease, there was an enhanced inflammatory airway response with the induction of an anti-viral and T-helper 1 and 2 (Th1/2) inflammatory response compared with healthy individuals. Individuals with COVID-19 who clinically deteriorated (ie, who met the primary outcome) showed an early blunted respiratory interferon response and pronounced and persistent Th2 inflammation, mediated by CC chemokine ligand (CCL)-24, compared with those with COVID-19 who did not clinically deteriorate. Over time, the natural course of COVID-19 showed persistently high respiratory interferon concentrations and elevated concentrations of the eosinophil chemokine, CCL-11, despite clinical symptom improvement. There was persistent systemic inflammation after 28 days following COVID-19, including elevated concentrations of interleukin (IL)-6, tumour necrosis factor-α, and CCL-11. Budesonide treatment modulated inflammation in the nose and blood and was shown to decrease IL-33 and increase CCL17. The STOIC trial was registered with ClinicalTrials.gov, NCT04416399.

Interpretation. An initial blunted interferon response and heightened T-helper 2 inflammatory response in the respiratory tract following SARS-CoV-2 infection could be a biomarker for predicting the development of severe COVID-19 disease. The clinical benefit of inhaled budesonide in early COVID-19 is likely to be as a consequence of its inflammatory modulatory effect, suggesting efficacy by reducing epithelial damage and an improved T-cell response.  
<https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00002-9/fulltext>

**title:** Inhaled corticosteroids: not just for asthma, but for COVID-19?

the lancet respiratory medicine| 7th april 2022  
  
A multipronged approach has been developed for the treatment of COVID-19 disease: antivirals and antibody therapy are effective during early infection when the SARS-CoV-2 load is high, whereas systemic steroids and cytokine blockade are best for the late inflammatory phase1 (figure). In human challenge studies of respiratory syncytial virus infection, the pre-existing so-called immunological tone of the respiratory mucosa is crucial to the receptiveness of the mucosa to viral infection.4 However, so far, in SARS-CoV-2 infection, there has been little focus on altering the condition of the respiratory mucosa. In this issue of The Lancet Respiratory Medicine, Jonathan R Baker and colleagues provide an update on the outcomes of the STOIC study showing that there is a distinctive nasal inflammatory response during the initial phase of infection, which might be altered by early administration of inhaled budesonide. This is important, since corticosteroid inhalers are widely used for asthma and are cheap, safe, and readily available…

…The findings of Baker and colleagues represent an important step towards improving our understanding of how local immune responses drive disease outcome in COVID-19, highlighting the need to consider treatments that target mucosal and systemic responses. Although the study provides evidence that inhaled budesonide might be beneficial in some cases of early COVID-19, further research is needed to understand exactly how this effect is mediated and which patients might benefit most.  
<https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00053-4/fulltext>

title: Systemic Corticosteroid Use for COVID-19 in US Outpatient Settings From April 2020 to August 2021 [research letter]  
  
jama| 8th april 2022  
  
In June 2020, preliminary results for the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial conducted in the UK indicated benefit from dexamethasone in severely ill hospitalized patients with COVID-19 but potential harm in those not requiring oxygen.1,2 In October 2020, the National Institutes of Health (NIH) issued COVID-19 treatment guidelines advising against systemic corticosteroid use in patients with mild to moderate COVID-19.1 Using 2 large US health care claims databases, we examined systemic corticosteroid use among nonhospitalized patients with COVID-19…

…Despite NIH recommendations, increasing numbers of nonhospitalized patients with COVID-19 were prescribed systemic corticosteroids, often on the day of diagnosis. Use appeared to be more prominent in the South and was not restricted to older patients. Limitations of the study included inability to capture date of symptom onset and indication for use, and potential for misclassifying mild to moderate COVID-19 disease due to overburdened resources and limited ability to accurately capture elements to define disease severity, including oxygen use. Given the increasing use of corticosteroids through August 2021, the potential safety signal,2,5,6 and the lack of efficacy data in patients with mild to moderate COVID-19,1 it is critical that prescribers consider the NIH guidelines in the therapeutic management of nonhospitalized patients with COVID-19.  
<https://jamanetwork.com/journals/jama/fullarticle/2791078>

**title:** Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19

new england journal of medicine | 14th april 2022  
  
BACKGROUND. Nirmatrelvir is an orally administered severe acute respiratory syndrome coronavirus 2 main protease (Mpro) inhibitor with potent pan–human-coronavirus activity in vitro.

METHODS. We conducted a phase 2–3 double-blind, randomized, controlled trial in which symptomatic, unvaccinated, nonhospitalized adults at high risk for progression to severe coronavirus disease 2019 (Covid-19) were assigned in a 1:1 ratio to receive either 300 mg of nirmatrelvir plus 100 mg of ritonavir (a pharmacokinetic enhancer) or placebo every 12 hours for 5 days. Covid-19–related hospitalization or death from any cause through day 28, viral load, and safety were evaluated.

RESULTS. A total of 2246 patients underwent randomization; 1120 patients received nirmatrelvir plus ritonavir (nirmatrelvir group) and 1126 received placebo (placebo group). In the planned interim analysis of patients treated within 3 days after symptom onset (modified intention-to treat population, comprising 774 of the 1361 patients in the full analysis population), the incidence of Covid-19–related hospitalization or death by day 28 was lower in the nirmatrelvir group than in the placebo group by 6.32 percentage points (95% confidence interval [CI], −9.04 to −3.59; P<0.001; relative risk reduction, 89.1%); the incidence was 0.77% (3 of 389 patients) in the nirmatrelvir group, with 0 deaths, as compared with 7.01% (27 of 385 patients) in the placebo group, with 7 deaths. Efficacy was maintained in the final analysis involving the 1379 patients in the modified intention-to-treat population, with a difference of −5.81 percentage points (95% CI, −7.78 to −3.84; P<0.001; relative risk reduction, 88.9%). All 13 deaths occurred in the placebo group. The viral load was lower with nirmatrelvir plus ritonavir than with placebo at day 5 of treatment, with an adjusted mean difference of −0.868 log10 copies per milliliter when treatment was initiated within 3 days after the onset of symptoms. The incidence of adverse events that emerged during the treatment period was similar in the two groups (any adverse event, 22.6% with nirmatrelvir plus ritonavir vs. 23.9% with placebo; serious adverse events, 1.6% vs. 6.6%; and adverse events leading to discontinuation of the drugs or placebo, 2.1% vs. 4.2%). Dysgeusia (5.6% vs. 0.3%) and diarrhea (3.1% vs. 1.6%) occurred more frequently with nirmatrelvir plus ritonavir than with placebo.

CONCLUSIONS. Treatment of symptomatic Covid-19 with nirmatrelvir plus ritonavir resulted in a risk of progression to severe Covid-19 that was 89% lower than the risk with placebo, without evident safety concerns.  
<https://www.nejm.org/doi/full/10.1056/NEJMoa2118542>

**title:** Risk of adverse events after covid-19 in Danish children and adolescents and effectiveness of BNT162b2 in adolescents: cohort study

bmj| 11th april 2022  
  
Objectives To assess the risk of acute and post-acute adverse events after SARS-CoV-2 infection in children and adolescents in Denmark and to evaluate the real world effectiveness of the BNT162b2 mRNA vaccine (Pfizer-BioNTech) among adolescents.

Design Cohort study. Setting Nationwide Danish healthcare registers. Participants All Danish people younger than 18 years who were either tested for SARS-CoV-2 using reverse transcriptase polymerase chain reaction (RT-PCR) or vaccinated with BNT162b2 to 1 October 2021.

Main outcome measures Risk of hospital admissions (any hospital contact of ≥12 hours); intensive care unit (ICU) admissions; serious complications, including multisystem inflammatory syndrome in children (MIS-C), myocarditis, and neuroimmune disorders; and initiating drug treatment and health service use up to six months after being tested. Vaccine effectiveness in vaccine recipients compared with unvaccinated peers was evaluated as one minus the risk ratio at 20 days after the first dose and 60 days after the second dose.

Results Of 991 682 children and adolescents tested for SARS-CoV-2 using RT-PCR in Denmark, 74 611 (7.5%) were positive. The risk of hospital admission with any variant for ≥12 hours was 0.49% (95% confidence interval 0.44% to 0.54%; 361/74 350), and 0.01% (0.01% to 0.03%; 10/73 187) of participants were admitted to an ICU within 30 days of testing positive. The risk of MIS-C within two months of SARS-CoV-2 infection was 0.05% (0.03% to 0.06%; 32/70 666), whereas no participants had myocarditis outside of MIS-C or encephalitis and fewer than five had Guillain-Barré syndrome. In the post-acute phase (1-6 months after infection), participants who tested positive for SARS-CoV-2 showed a 1.08-fold (95% confidence interval 1.06-fold to 1.10-fold) increase in rate of contacts with general practitioners compared with a reference cohort sampled among all children tested for SARS-CoV-2 during the study period. Overall, 278 649 adolescents received BNT162b2. Compared with unvaccinated adolescents, the estimated vaccine effectiveness among 229 799 adolescents vaccinated with one dose was 62% (95% confidence interval 59% to 65%) after 20 days, and among 175 176 vaccinated with two doses was 93% (92% to 94%) after 60 days during a period when delta was the dominant variant.

Conclusions The absolute risks of adverse events after SARS-CoV-2 infection were generally low in Danish children and adolescents, although MIS-C occurred in 0.05% (32/70 666) of participants with RT-PCR confirmed SARS-CoV-2 infection. In adjusted analyses, rates of general practitioner visits were slightly increased in SARS-CoV-2 positive children and adolescents, which could indicate persisting symptoms. BNT162b2 appeared to be effective in reducing the risk of SARS-CoV-2 infection with the delta variant in adolescents.  
<https://www.bmj.com/content/377/bmj-2021-068898>

**title:** Breakthrough SARS-CoV-2 Infections, Hospitalizations, and Mortality in Vaccinated Patients With Cancer in the US Between December 2020 and November 2021

jama oncology| 8th april 2022  
  
Question What are the time trends, risks, and outcomes of breakthrough SARS-CoV-2 infections in vaccinated patients with cancer in the US between December 2020 and November 2021?

Findings In this cohort study of a nationwide database of electronic health records of 636 465 vaccinated patients, the 45 253 vaccinated patients with cancer had significantly higher risk for breakthrough SARS-CoV-2 infections than propensity score–matched patients without cancer, with marked heterogeneity among 12 common cancers, including solid tumors and hematologic cancers, most common in patients with active cancer within the past year. Breakthrough infections in patients with cancer were associated with significant and substantial risks for hospitalizations and mortality.

Meaning With the emergence of SARS-CoV-2 virus variants and the waning immunity of vaccines, the findings raise the consideration for the development and implementation of enhanced mitigation strategies in vaccinated patients with specific cancers, especially those undergoing active cancer care.  
<https://jamanetwork.com/journals/jamaoncology/fullarticle/2791076>

**title:** Antibiotic Prescriptions Associated With COVID-19 Outpatient Visits Among Medicare Beneficiaries, April 2020 to April 2021 [research letter]

jama | 8th april 2022  
  
Antibiotics are ineffective treatment for viral syndromes, including COVID-19. We characterized antibiotic prescribing in older adults with outpatient COVID-19 visits to identify opportunities to improve prescribing practices.

Methods. We used 100% Medicare carrier claims and Part D event files to identify beneficiaries with a COVID-19 outpatient visit and associated antibiotic prescriptions. We included beneficiaries aged 65 years and older who had fee-for-service plus Part D coverage and a visit during April 2020 to April 2021. We identified telehealth visits with Current Procedural Terminology codes1 and in-person visits (office, urgent care, and emergency department [ED]) with place-of-service codes. To identify visits with a primary diagnosis of COVID-19, we first limited them to those with International Classification of Diseases and Related Health Problems, 10th Revision diagnosis code U07.1. We then excluded visits with additional diagnosis codes for conditions for which antibiotics are always or sometimes appropriate based on clinical guidelines using a previously described tiered system.2 Visits were then linked to an antibiotic if prescribed within 7 days before or after the visit. We reported visits by setting and month, including antibiotic classes.

We performed 2-sided χ2 tests to compare the distribution of characteristics between beneficiaries with COVID-19 who were and were not prescribed an antibiotic by age, sex, race, and prescribers’ location. This study was deemed nonhuman subjects research by the Centers for Disease Control and Prevention and did not require institutional review board review. Analyses were performed in SAS version 9.4. P < .05 defined statistical significance.

Results. During April 2020 to April 2021, 346 204 (29.6%) of 1 169 120 COVID-19 outpatient visits were associated with an antibiotic prescription, which varied by month, with higher rates of antibiotic prescribing occurring during a wave of COVID-19 cases during the winter of 2020-2021 (range, 17.5% in May 2020 to 33.3% in October 2020) (Figure). Prescribing was highest in the ED (33.9%), followed by telehealth (28.4%), urgent care (25.8%), and office (23.9%) (Figure) visits. Azithromycin was the most frequently prescribed antibiotic (50.7%), followed by doxycycline (13.0%), amoxicillin (9.4%), and levofloxacin (6.7%). Urgent care had the highest percentage of azithromycin prescriptions (60.1%), followed by telehealth (55.7%), office (51.5%), and ED (47.4%). Differences were observed by age, sex, and location (Table). Non-Hispanic White beneficiaries received antibiotics for COVID-19 more frequently (30.6%) than other racial and ethnic groups: American Indian/Alaska Native (24.1%), Asian/Pacific Islander (26.5%), Black or African American (23.2%), and Hispanic (28.8%) (Table).

Discussion. During the first year of the COVID-19 pandemic, 30% of outpatient visits for COVID-19 among Medicare beneficiaries were linked to an antibiotic prescription, 50.7% of which were for azithromycin. Randomized clinical trials demonstrated no benefit of azithromycin in treating COVID-19,3,4 and its use for the disease has been linked to antimicrobial resistance.5 The largest number of visits and highest rates of antibiotic prescribing were observed in the ED, perhaps reflecting acuity of care, and urgent care centers had the highest rate of azithromycin prescribing. Telehealth visits had the second highest antibiotic prescribing rate and were close in volume to office visits, emphasizing the importance of optimizing antibiotic prescribing practices in this setting. Antibiotic prescribing occurred at a higher rate for non-Hispanic White beneficiaries than for those from other racial and ethnic groups. Although described in pediatrics, this racial difference has not been well characterized in older adults and warrants further evaluation because it may indicate more services are being provided to White beneficiaries, even if not indicated.

Study limitations include that, although only visits for which COVID-19 was the primary diagnosis were included and visits with a diagnosis code that putatively justified an antibiotic were excluded, misclassification was possible. Underlying chronic medical conditions or severity of illness and subsequent hospital admission were not controlled for. These data may not be representative of the entire US population nor adults aged 65 years and older without Medicare prescription drug coverage. Data since April 2021 were not available, and strong evidence against azithromycin use was not published until the end of the observation period.

These observations reinforce the importance of improving appropriate antibiotic prescribing in outpatient settings and avoiding unnecessary antibiotic use for viral infections such as COVID-19 in older adult populations.  
<https://jamanetwork.com/journals/jama/fullarticle/2791077>

**title:** Necrotic Plaques on the Ears of a Patient With COVID-19

jama dermatology| 5th april 2022  
  
A man in his 40s with a medical history of factor VII deficiency hemophilia presented with acute hypoxic respiratory failure secondary to COVID-19. Following admission, he was intubated with prone positioning, and treatment with tocilizumab and dexamethasone was started. He was also found to have Staphylococcus hemolyticus bacteremia, and treatment with cefepime was initiated. Three days after admission, the patient developed erythema and edematous necrotic plaques of the bilateral ears (Figure, A and B). No devices had been used on the ears…  
<https://jamanetwork.com/journals/jamadermatology/article-abstract/2790789>

**title:** Postmortem Assessment of Olfactory Tissue Degeneration and Microvasculopathy in Patients With COVID-19

jama neurology| 11th april 2022  
  
Question What are the neuropathologic changes of COVID-19 in the olfactory region?

Findings In this cohort study of 23 deceased patients with COVID-19 and 14 matched controls, more severe axon pathology, axon losses, and microvascular pathology were noted in olfactory tissue from patients with COVID-19 than that from the control individuals. The olfactory pathology was particularly severe in patients with reported smell alterations but were not associated with the clinical severity, timing of infection, or the presence of SARS-CoV-2 in the olfactory tissue.

Meaning In the region of olfactory bulb and olfactory tract, COVID-19 infection was associated with axon pathology and microvasculopathy, particularly in patients with smell alterations; the olfactory pathology did not result from direct viral injury and may be associated with local inflammation.  
<https://jamanetwork.com/journals/jamaneurology/fullarticle/2790735>

**rates and variants**

**title:** Covid-19: Symptomatic infection with omicron variant is milder and shorter than with delta, study reports  
  
bmj | 7th april 2022  
  
Vaccinated people infected with the omicron variant of SARS-CoV-2 had symptoms for 6.87 days on average, compared with 8.89 days with the delta variant, data from the ZOE app have shown.1 Among those who had received two vaccine doses plus a booster the duration of symptoms was shorter still, at 4.4 days with omicron and 7.7 days with delta. The shorter presentations of symptoms suggest a shorter period of infectiousness with omicron, which could affect workplace health policies and public health guidance, said the study authors from King’s College, London. However, this will need to be confirmed by viral load studies.

The large community cohort study, published in the Lancet,1 also found that patients infected with the omicron variant reported a loss of smell less frequently and were more likely to have a sore throat and a hoarse voice than those infected with the delta variant. The UK’s official list of covid-19 symptoms has now been expanded to include sore throat, fatigue, headache, and six other symptoms.2 The team behind the ZOE app and others had been lobbying for some time to get the original list of three symptoms updated.

For the latest study, researchers identified 63 002 people who had self-reported test results and symptoms using the ZOE covid app. They were aged 16 to 99, were based in the UK with a body mass index of 15 to 55, had received at least two doses of any SARS-CoV-2 vaccine, were symptomatic, and had logged a positive PCR or lateral flow test for SARS-CoV-2. A matched sample of 4999 participants who were infected during a period when delta was prevalent (1 June 2021 to 27 November 2021) was then compared with 4999 participants infected when omicron was dominant in the UK (20 December 2021 to 17 January 2022).

Study findings. Loss of smell was less common in people infected during the omicron wave than during the delta wave (16.7% v 52.7%; odds ratio 0.17 (95% confidence interval 0.16 to 0.19); P<0.001). Sore throat was more common during omicron prevalence than delta prevalence (70.5% v 60.8%; 1.55 (1.30 to 1.69); P<0.001). Patients infected with the omicron variant were also found to be 24% more likely to develop a hoarse voice than those with delta. And those infected during the omicron wave were around half as likely to display at least one of the three “classic” covid-19 symptoms (fever, loss of smell, and persistent cough) than people infected with delta.

The study also found that patients infected during the omicron wave were 25% less likely to be admitted to hospital (1.9%) than patients infected during the period of high delta prevalence (2.6%). Patients infected during the omicron wave were also 2.5 times more likely to recover within one week than patients with delta.

The research confirms earlier studies from South Africa and South Korea, which suggested that infection with the omicron variant was notably less severe than with the previous dominant variants.

Tim Spector, one of the study authors, told The BMJ, “The UK has now updated its list of symptoms but has not issued any proper guidance on how this should be used or observed. Also, the order in which they are presented is still misleading, as it suggests the classical symptoms are still the most important, when in fact they are the minority of symptoms and often only appear after several days of infection.” He added that the shorter duration of symptoms with omicron versus delta confirmed that five days was about the right length of time for people to isolate if they have symptoms.

Easy-to-use apps. One limitation of the study is that the researchers were unable to compare symptoms, risk of hospital admission, or duration of infection by the two variants in unvaccinated people, as most participants were vaccinated. Also, hospital admission was not ascertained from surveillance systems but was self-reported. Additionally, infection with omicron and delta was assigned on the basis of prevalence in the UK population at the time and not on individual sequencing from these participants.

In an accompanying commentary Linda Houhamdi and Pierre-Edouard Fournier, of the University of Aix-Marseille Université and Assistance Publique-Hôpitaux de Marseille in France, wrote that large scale tracking apps such as ZOE were very useful monitoring tools. They said, “The severity of this disease and the unprecedented ability of SARS-CoV-2 to modify its genome and spread in successive waves highlights the usefulness of easy-to-use mobile apps such as ZOE to rapidly assess the characteristics of a new variant and implement optimised management measures.”  
<https://www.bmj.com/content/377/bmj.o922>

**title:** Comparable neutralisation evasion of SARS-CoV-2 omicron subvariants BA.1, BA.2, and BA.3  
  
the lancet infectious diseases|12th april 2022  
  
Background. Severe COVID-19 T-cell lymphopenia is more common among older adults and entails   
The SARS-CoV-2 omicron (B.1.1.529) variant has rapidly become globally dominant, displacing the previously dominant delta (B1.617.2) variant. The viral spike (S) protein is the key target of the neutralising antibody response, and the omicron variant harbours more than 35 mutations in the S protein, which allow highly efficient evasion from neutralising antibodies.1

In keeping with these findings, the omicron variant efficiently spreads in populations with a high percentage of convalescent or vaccinated individuals.2

The three main subvariants of the omicron variant are BA.1, BA.2, and BA.3. Initial data suggest that BA.2 might have a growth advantage over BA.1 posing a rapidly increasing threat to health systems. The omicron subvariants display remarkable differences regarding S protein mutations, particularly with respect to the N-terminal domain and the receptor-binding domain (appendix pp 2–3), which are known to harbour key epitopes of neutralising antibodies. Here, we compared BA.1, BA.2, and BA.3 for sensitivity to neutralisation by antibodies induced by infection and vaccination, using pseudoviruses as a model system, which adequately mirrors SARS-CoV-2 neutralisation by antibodies…  
<https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00224-9/fulltext>

**title:** Estimating global, regional, and national daily and cumulative infections with SARS-CoV-2 through Nov 14, 2021: a statistical analysis  
  
the lancet| 8th april 2022  
  
Timely, accurate, and comprehensive estimates of SARS-CoV-2 daily infection rates, cumulative infections, the proportion of the population that has been infected at least once, and the effective reproductive number (Reffective) are essential for understanding the determinants of past infection, current transmission patterns, and a population's susceptibility to future infection with the same variant. Although several studies have estimated cumulative SARS-CoV-2 infections in select locations at specific points in time, all of these analyses have relied on biased data inputs that were not adequately corrected for. In this study, we aimed to provide a novel approach to estimating past SARS-CoV-2 daily infections, cumulative infections, and the proportion of the population infected, for 190 countries and territories from the start of the pandemic to Nov 14, 2021. This approach combines data from reported cases, reported deaths, excess deaths attributable to COVID-19, hospitalisations, and seroprevalence surveys to produce more robust estimates that minimise constituent biases.

Methods. We produced a comprehensive set of global and location-specific estimates of daily and cumulative SARS-CoV-2 infections through Nov 14, 2021, using data largely from Johns Hopkins University (Baltimore, MD, USA) and national databases for reported cases, hospital admissions, and reported deaths, as well as seroprevalence surveys identified through previous reviews, SeroTracker, and governmental organisations. We corrected these data for known biases such as lags in reporting, accounted for under-reporting of deaths by use of a statistical model of the proportion of excess mortality attributable to SARS-CoV-2, and adjusted seroprevalence surveys for waning antibody sensitivity, vaccinations, and reinfection from SARS-CoV-2 escape variants. We then created an empirical database of infection–detection ratios (IDRs), infection–hospitalisation ratios (IHRs), and infection–fatality ratios (IFRs). To estimate a complete time series for each location, we developed statistical models to predict the IDR, IHR, and IFR by location and day, testing a set of predictors justified through published systematic reviews. Next, we combined three series of estimates of daily infections (cases divided by IDR, hospitalisations divided by IHR, and deaths divided by IFR), into a more robust estimate of daily infections. We then used daily infections to estimate cumulative infections and the cumulative proportion of the population with one or more infections, and we then calculated posterior estimates of cumulative IDR, IHR, and IFR using cumulative infections and the corrected data on reported cases, hospitalisations, and deaths. Finally, we converted daily infections into a historical time series of Reffective by location and day based on assumptions of duration from infection to infectiousness and time an individual spent being infectious. For each of these quantities, we estimated a distribution based on an ensemble framework that captured uncertainty in data sources, model design, and parameter assumptions.

Findings. Global daily SARS-CoV-2 infections fluctuated between 3 million and 17 million new infections per day between April, 2020, and October, 2021, peaking in mid-April, 2021, primarily as a result of surges in India. Between the start of the pandemic and Nov 14, 2021, there were an estimated 3·80 billion (95% uncertainty interval 3·44–4·08) total SARS-CoV-2 infections and reinfections combined, and an estimated 3·39 billion (3·08–3·63) individuals, or 43·9% (39·9–46·9) of the global population, had been infected one or more times. 1·34 billion (1·20–1·49) of these infections occurred in south Asia, the highest among the seven super-regions, although the sub-Saharan Africa super-region had the highest infection rate (79·3 per 100 population [69·0–86·4]). The high-income super-region had the fewest infections (239 million [226–252]), and southeast Asia, east Asia, and Oceania had the lowest infection rate (13·0 per 100 population [8·4–17·7]). The cumulative proportion of the population ever infected varied greatly between countries and territories, with rates higher than 70% in 40 countries and lower than 20% in 39 countries. There was no discernible relationship between Reffective and total immunity, and even at total immunity levels of 80%, we observed no indication of an abrupt drop in Reffective, indicating that there is not a clear herd immunity threshold observed in the data.

Interpretation. COVID-19 has already had a staggering impact on the world up to the beginning of the omicron (B.1.1.529) wave, with over 40% of the global population infected at least once by Nov 14, 2021. The vast differences in cumulative proportion of the population infected across locations could help policy makers identify the transmission-prevention strategies that have been most effective, as well as the populations at greatest risk for future infection. This information might also be useful for targeted transmission-prevention interventions, including vaccine prioritisation. Our statistical approach to estimating SARS-CoV-2 infection allows estimates to be updated and disseminated rapidly on the basis of newly available data, which has and will be crucially important for timely COVID-19 research, science, and policy responses.  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00484-6/fulltext>

**title:** How to interpret the total number of SARS-CoV-2 infections  
  
the lancet| 8th april 2022  
  
Counts of reported cases have been the key metric to monitor the COVID-19 pandemic. However, since the beginning, it has been clear that reported cases represent only a fraction of all SARS-CoV-2 infections.1

In The Lancet, Ryan Barber and colleagues, writing on behalf of the Institute for Health Metrics and Evaluation, report a comprehensive set of global and location-specific estimates of daily and cumulative SARS-CoV-2 infections and the proportion of the population infected for 190 countries and territories up to Nov 14, 2021.

For this, the authors used a novel approach, combining data from reported cases and deaths, excess deaths attributable to COVID-19, hospitalisations, and seroprevalence surveys to produce more robust estimates in an attempt to minimise biases. According to Barber and colleagues' findings, a staggering number of people, 3·39 billion (95% uncertainty interval 3·08–3·63) or 43·9% (39·9–46·9) of the global population, are estimated to have been infected one or more times between March, 2020, and November, 2021. Remarkably, this was before the highly transmissible omicron (B.1.1.529) variant swept the globe. These estimates of total infections are wildly different from the number of reported cases, which stood at 254 million as of Nov 14, 2021.

Barber and colleagues' study also highlights vast regional discrepancies, painting a very different picture from that provided by reported cases. From case reports, one would conclude that the highest cumulative incidence was observed in Europe and North America and the lowest in Africa. However, this study estimated that 70·5% (61·6–75·9) of the population in sub-Saharan Africa has been infected with SARS-CoV-2, compared with 30·9% (28·8–32·8) of the population in high-income North America. Underlying this apparent reversal of patterns are stark differences in case detection; fewer than 1% of infections were reported as cases in sub-Saharan Africa whereas nearly half were reported in high-income North America. It is crucial that this underreporting is considered when we compare the impact of the pandemic and the effectiveness of responses among nations.

It is also worth reflecting on the technical achievement in data integration that underpins these new estimates. Barber and colleagues were able to estimate cumulative infections at the national and subnational levels by integrating an array of data sources. Each individual dataset—cross-sectional serosurveys and time series of cases, hospitalisations, and deaths—has limited value and inherent bias on its own. Serosurveys are of highly variable quality, death reporting is incomplete,4 and many outcomes are not reliably stratified by age or other key variables such as gender, race, and vaccination status. Despite the serious challenges in data integration on this scale and with this diversity of sources, it enables objective comparisons about the level of infection in a setting and can, for example, guide more optimal targeting of vaccines.

Although estimates of the proportion of the population ever infected provide insight into the cumulative impact and current phase of the epidemic in each location, we should be cautious not to conflate the proportion of the population ever infected with population-level immunity. The proportion ever infected, combined with vaccine coverage, has been proposed as a metric to evaluate whether we have reached sufficient population immunity to stop widespread community transmission. However, with new variants escaping immunity, immunity waning, and unequal distribution of vaccination, defining population-level immunity is not trivial.

Barber and colleagues' study estimated population immunity in the simplest way possible: by assuming that previously infected people were immune, vaccination was randomly distributed, and immunity did not wane. Tellingly, this metric did not inversely correlate with community transmission (ie, the time-varying reproductive number), showing that such a simple approach no longer provides an appropriate measure of population immunity. A more reliable measure would account for waning, boosting from multiple exposures, non-random vaccine uptake, different immune response across age groups, and cross-variant immunity.

As such, one could argue that the proportion of the population ever infected is no longer a meaningful metric of population immunity. However, the same data streams to infer cumulative incidence can be used to address more pressing epidemiological questions, such as how severe are new variants? To what extent do the population's historical infections—in terms of timing and variants—protect against infection and severe disease of new variants? Relatedly, how do layers of vaccine-induced and virus-induced immunity combine to confer protection to the population? Perhaps most importantly at this moment in the pandemic, we need to identify the sub-populations that remain susceptible to severe disease and death. Serosurveys combined with morbidity and mortality surveillance and detailed monitoring of vaccine coverage are essential to identify the groups lacking immunity from vaccination or previous infection.5 Integrating data enables the kinds of insights offered by Barber and colleagues to inform the next phase of the pandemic response, and we should sustain this effort.  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00629-8/fulltext>

**title:** Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of omicron and delta variant dominance: a prospective observational study from the ZOE COVID Study  
  
the lancet|7th april 2022  
  
Background. The SARS-CoV-2 variant of concern, omicron, appears to be less severe than delta. We aim to quantify the differences in symptom prevalence, risk of hospital admission, and symptom duration among the vaccinated population.

Methods. In this prospective longitudinal observational study, we collected data from participants who were self-reporting test results and symptoms in the ZOE COVID app (previously known as the COVID Symptoms Study App). Eligible participants were aged 16–99 years, based in the UK, with a body-mass index between 15 and 55 kg/m2, had received at least two doses of any SARS-CoV-2 vaccine, were symptomatic, and logged a positive symptomatic PCR or lateral flow result for SARS-CoV-2 during the study period. The primary outcome was the likelihood of developing a given symptom (of the 32 monitored in the app) or hospital admission within 7 days before or after the positive test in participants infected during omicron prevalence compared with those infected during delta prevalence.

Findings. Between June 1, 2021, and Jan 17, 2022, we identified 63 002 participants who tested positive for SARS-CoV-2 and reported symptoms in the ZOE app. These patients were matched 1:1 for age, sex, and vaccination dose, across two periods (June 1 to Nov 27, 2021, delta prevalent at >70%; n=4990, and Dec 20, 2021, to Jan 17, 2022, omicron prevalent at >70%; n=4990). Loss of smell was less common in participants infected during omicron prevalence than during delta prevalence (16·7% vs 52·7%, odds ratio [OR] 0·17; 95% CI 0·16–0·19, p<0·001). Sore throat was more common during omicron prevalence than during delta prevalence (70·5% vs 60·8%, 1·55; 1·43–1·69, p<0·001). There was a lower rate of hospital admission during omicron prevalence than during delta prevalence (1·9% vs 2·6%, OR 0·75; 95% CI 0·57–0·98, p=0·03).

Interpretation. The prevalence of symptoms that characterise an omicron infection differs from those of the delta SARS-CoV-2 variant, apparently with less involvement of the lower respiratory tract and reduced probability of hospital admission. Our data indicate a shorter period of illness and potentially of infectiousness which should impact work–health policies and public health advice.  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00327-0/fulltext>

**title:** Population Immunity and Covid-19 Severity with Omicron Variant in South Africa  
  
new england journal of medicine|7th april 2022  
  
Background. The B.1.1.529 (omicron) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified on November 25, 2021, in Gauteng province, South Africa. Data regarding the seroprevalence of SARS-CoV-2 IgG in Gauteng before the fourth wave of coronavirus disease 2019 (Covid-19), in which the omicron variant was dominant, are needed.

Methods. We conducted a seroepidemiologic survey from October 22 to December 9, 2021, in Gauteng to determine the seroprevalence of SARS-CoV-2 IgG. Households included in a previous seroepidemiologic survey (conducted from November 2020 to January 2021) were contacted; to account for changes in the survey population, there was a 10% increase in the households contacted, with the use of the same sampling framework. Dried-blood-spot samples were tested for IgG against SARS-CoV-2 spike protein and nucleocapsid protein with the use of quantitative assays. We also evaluated Covid-19 epidemiologic trends in Gauteng, including cases, hospitalizations, recorded deaths, and excess deaths from the start of the pandemic through January 12, 2022.

Results. Samples were obtained from 7010 participants, of whom 1319 (18.8%) had received a Covid-19 vaccine. The seroprevalence of SARS-CoV-2 IgG ranged from 56.2% (95% confidence interval [CI], 52.6 to 59.7) among children younger than 12 years of age to 79.7% (95% CI, 77.6 to 81.5) among adults older than 50 years of age. Vaccinated participants were more likely to be seropositive for SARS-CoV-2 than unvaccinated participants (93.1% vs. 68.4%). Epidemiologic data showed that the incidence of SARS-CoV-2 infection increased and subsequently declined more rapidly during the fourth wave than it had during the three previous waves. The incidence of infection was decoupled from the incidences of hospitalization, recorded death, and excess death during the fourth wave, as compared with the proportions seen during previous waves.

Conclusions. Widespread underlying SARS-CoV-2 seropositivity was observed in Gauteng before the omicron-dominant wave of Covid-19. Epidemiologic data showed a decoupling of hospitalizations and deaths from infections while omicron was circulating.  
<https://www.nejm.org/doi/full/10.1056/NEJMoa2119658>

**infection control**

**title:** Covid-19 testing in the UK was not a “shambles” in 2020  
  
BMJ|12th april 2022  
  
In a recent interview with The BMJ, Paul Nurse said that covid-19 PCR testing in the UK in 2020 was a shambles.1 I respond as someone who volunteered to help set up the Milton Keynes Lighthouse testing laboratory….  
<https://www.bmj.com/content/377/bmj.o916.full>

**title:** Helen Salisbury: Why we still need to test for covid-19  
  
BMJ| 12th april 2022

Background. Real-world evidence supporting vaccination against COVID-19 in individuals who have   
There are many situations in general practice where history and examination alone are enough to make a confident diagnosis without the need for investigations. We can diagnose menopause or mechanical low back pain without blood tests or scans, and we can often advise on the management of self-limiting minor complaints without ever knowing the exact cause. On other occasions, however, I really don’t know what I’m dealing with until test results appear in my inbox.

It’s been over a year since clinicians and researchers began calling for the UK government to widen the official list of symptoms of covid-19 beyond fever, continuous cough, and loss of taste and smell.12 That change has finally been made, just as widespread free testing ended, which is an odd coincidence. The UK’s official list now acknowledges that the SARS-CoV-2 virus may cause many and varied symptoms, including fatigue, myalgia, headache, loss of appetite, vomiting, and diarrhoea.3 This is not news to those of us working in healthcare, but it may well be to the general public.

When people consult a GP with these non-specific symptoms it would be useful to know if they do have covid. Most of us remember being asked as junior doctors to justify investigations: “And how will the result change your management?” is a question that still rings in my ears. It’s worth asking here. Firstly, if my patient is vulnerable or unvaccinated I’ll need to follow them up proactively and possibly supply them with an oxygen saturation meter, as they may be at risk of deterioration. Secondly, if we have a diagnosis we can stop looking for other causes. Thirdly, patients need to know whether they should self-isolate to protect family, friends, and colleagues. They may also need proof of infection if they’re one of the unlucky ones who develop long covid—1.7 million people in the UK at present, or 2.7% of the population.4 The final reason I need to test for any infectious disease is to inform the public health response (although, when it comes to covid, I’m not sure that we still have one). With other infectious diseases I can order a test for my patients, but I can’t do so for covid, and I have an eerie (and weary) sense of déjà vu.5 Since the end of widespread free testing on 1 April it’s still possible for patients to request a test online if they’ve been advised to by their GP. As data from the Office for National Statistics suggest that one in 13 people in England currently has covid, I suspect that GPs around the country will be very busy giving them this advice.4 The solution would be to reverse the illogical decision to end free testing at a time when infection rates are the highest they’ve ever been.4 Surely we haven’t already spent all of the “eye wateringly” large sums of money that were set aside for this purpose?  
<https://www.bmj.com/content/377/bmj.o951>

**title:** COVID-19 vaccine waning and effectiveness and side-effects of boosters: a prospective community study from the ZOE COVID Study

the lancet infectious diseases| 8th april 2022  
  
Background. With the surge of new SARS-CoV-2 variants, countries have begun offering COVID-19 vaccine booster doses to high-risk groups and, more recently, to the adult population in general. However, uncertainty remains over how long primary vaccination series remain effective, the ideal timing for booster doses, and the safety of heterologous booster regimens. We aimed to investigate COVID-19 primary vaccine series effectiveness and its waning, and the safety and effectiveness of booster doses, in a UK community setting.

Methods. We used SARS-CoV-2 positivity rates in individuals from a longitudinal, prospective, community-based study (ZOE COVID Study), in which data were self-reported through an app, to assess the effectiveness of three COVID-19 vaccines (ChAdOx1 nCov19 [Oxford-AstraZeneca], BNT162b2 [Pfizer-BioNtech], and mRNA1273 [Moderna]) against infection in the 8 months after completion of primary vaccination series. In individuals receiving boosters, we investigated vaccine effectiveness and reactogenicity, by assessing 16 self-reported systemic and localised side-effects. We used multivariate Poisson regression models adjusting for confounders to estimate vaccine effectiveness.

Findings. We included 620 793 participants who received two vaccine doses (204 731 [33·0%] received BNT162b2, 405 239 [65·3%] received ChAdOx1 nCoV-19, and 10 823 [1·7%] received mRNA-1273) and subsequently had a SARS-CoV-2 test result between May 23 (chosen to exclude the period of alpha [B.1.1.7] variant dominance) and Nov 23, 2021. 62 172 (10·0%) vaccinated individuals tested positive for SARS-CoV-2 and were compared with 40 345 unvaccinated controls (6726 [16·7%] of whom tested positive). Vaccine effectiveness waned after the second dose: at 5 months, BNT162b2 effectiveness was 82·1% (95% CI 81·3–82·9), ChAdOx1 nCoV-19 effectiveness was 75·7% (74·9–76·4), and mRNA-1273 effectiveness was 84·3% (81·2–86·9). Vaccine effectiveness decreased more among individuals aged 55 years or older and among those with comorbidities. 135 932 individuals aged 55 years or older received a booster (2123 [1·6%] of whom tested positive). Vaccine effectiveness for booster doses in 0–3 months after BNT162b2 primary vaccination was higher than 92·5%, and effectiveness for heterologous boosters after ChAdOx1 nCoV-19 was at least 88·8%. For the booster reactogenicity analysis, in 317 011 participants, the most common systemic symptom was fatigue (in 31 881 [10·1%] participants) and the most common local symptom was tenderness (in 187 767 [59·2%]). Systemic side-effects were more common for heterologous schedules (32 632 [17·9%] of 182 374) than for homologous schedules (17 707 [13·2%] of 134 637; odds ratio 1·5, 95% CI 1·5–1·6, p<0·0001).

Interpretation. After 5 months, vaccine effectiveness remained high among individuals younger than 55 years. Booster doses restore vaccine effectiveness. Adverse reactions after booster doses were similar to those after the second dose. Homologous booster schedules had fewer reported systemic side-effects than heterologous boosters.  
<https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00146-3/fulltext>

**title:** We need more support and less normalcy to stop airborne viruses

BMJ| 13th april 2022  
  
Governments should be investing in a thorough redesign of how our air is filtered in public spaces, says Abraar Karan

…In the United States and Europe, there have been major pushes to have the public return to “normal,” an unclear gesture suggesting perhaps a world before covid-19. But this is a false promise, and is instead a justification for perpetuating the conditions that left many countries so vulnerable to covid-19 to begin with. Key among these are the inequities that have seen people live through strikingly different experiences of the pandemic.

For instance, isolating at home may pose notably lower risks if you are wealthy and health literate. You may have extra rooms where family members can self-isolate—a study from the US Centers for Disease Control and Prevention showed that having the ability to isolate in a separate room was associated with significantly lower odds of transmitting covid to family members during the omicron surge.2 You may be able to afford HEPA filters—studies have shown that higher levels of infectious aerosols in the air are associated with higher risk of transmission to others.3 You may have the time and knowledge to procure high filtration N95 masks for everyone in your home. And, through these efforts, you may very well avoid the rest of your family getting sick with covid-19. In addition, if you work in a job that can be done from home, you may be right back to getting your paycheck without having to wait in isolation.

Now consider if you were living in a small, crowded home or apartment where isolating in a separate room is not possible. Imagine if you did not have the funds to buy a portable HEPA filter; did not have the knowledge about how to construct low cost air filtration devices4; and worked a job in which you were on the frontlines and could not simply continue it from home. Tack on to this the possibility you did not receive paid time off from work and you are left now with the choice of whether to work while sick, or be both sick and unpaid.

Many patients who I treated had to make these choices. Many infected their entire families. Many died or were left with ongoing health complications. And the data reflect this as well. In a study of low income, primarily Hispanic families, household transmission of SARS-CoV-2 was found to be much higher than in most other studies examining the general population; and risk of disease spread was associated with lower household incomes…

…The answer is not to mask forever or to fall back on any of the other false, extreme dichotomies that are often presented. With an airborne virus, the impetus lies on the government to protect us all through a thorough redesign of how our air is filtered. In the hospital, when we are dealing with an airborne pathogen, we don’t just wear N95 masks. We also place those patients in rooms with increased air changes, HEPA filters, and in negative pressure rooms as well. Yet, for the general public, our leaders have focused mostly on masking and far less on the engineering controls that they could create to protect us. Just like we had revolutions in clean water or sewage disposal, or how we fundamentally improved roads when automobiles came into existence, so too must we revolutionise the cleaning of the air we share and breathe in public spaces. Anything short of this will fundamentally leave us vulnerable to this and future respiratory viruses.

Instead, the governments of many countries have turned responsibility over entirely to their citizens, advising them to mask (if they wish to) and get vaccinated. We know that masking can help reduce the spread of covid but as a strategy it is unsustainable indefinitely. We also know that while vaccines can protect us from severe disease, they are less effective in preventing infections,6 which when left unmitigated can cause catastrophic harms even if they have a lower fatality rate overall. So, we are left quibbling among ourselves about whether to mask or not, instead of demanding accountability from our governments to clean the air we breathe; ensure basic worker rights, such as paid time off for those who are sick; and more rigorously protect poorer families from in-home spread, through the provision of tools such as air purifiers/filters, rapid tests, and N95 masks when a family member is sick.

Covid-19 is not over. And, if nothing else, it should serve as a warning for how underprepared we are for future respiratory threats. This knowledge should not see us turning against one another, but looking towards our governments and leaders for the support we deserve.  
<https://www.bmj.com/content/377/bmj.o976>

**title:** Should we be clinically assessing antibody responses to covid vaccines in immunocompromised people?  
  
BMJ | 12th april 2022  
  
Serological testing to assess for a vaccine response would be a step towards providing more tailored care for immunocompromised people

The UK government has decreed that we must all now “live with covid.” All mandated isolation measures have ceased in England, free lateral flow testing for all has come to an end, and plans are in motion to scale back the surveillance programmes that have been instrumental in predicting covid waves, new variants, and vaccine efficacy. Notably absent from this bold strategy is practical guidance for the protection and mitigation of ongoing risk for people who were previously deemed to be clinically extremely vulnerable. This has left the 500 000 immunocompromised people in the UK, who have not been afforded the same level of protection from vaccination as the general population, feeling dispensable. In response to this abandonment, UK health charities have called on the government to give more support to those at highest risk from covid-19 so that they can live more normal lives.

Immunocompromised people have attenuated immune responses to covid-19 vaccines, which is clinically consistent with the higher rates of breakthrough infections and lower vaccine effectiveness seen in this population.2 This provided the rationale for the UK offering this group three primary vaccine doses plus a booster dose and, as was recently announced, a second spring booster dose (equating to a fifth dose for this population). Yet, to our knowledge, the UK has no immunogenicity data available from clinically vulnerable groups who’ve had four vaccine doses, which we could use to estimate the likely proportion of immunocompromised people who may not have protection against infection currently. Data from other countries suggests this may be a significant number, and if an individual has not had an immune response to four vaccine doses, in the absence of a change in immunosuppressed state, why would we expect that they will always mount a sufficient response to five? People whose immune systems haven’t responded to vaccines, and who remain unidentified outside of clinical trials, are expected to “live with covid” without mandated support from their employers or free access to testing for friends and family. Conversely, for those immunocompromised people who have had an immune response to four vaccine doses, reassurance that they will truly receive a “boost” in response to the fifth vaccine dose, will be a useful incentive for repeat inoculations…

…Many immunocompromised people undergo regular surveillance by hospital specialists, so the introduction of serological testing should not pose logistical concerns, although the appropriate timing of testing given waning antibodies would need to be considered, as would careful communication with immunocompromised people. One way of overcoming such challenges, if they were considered insurmountable, would be to introduce home testing via point of care kits or capillary sampling. In addition to logistical difficulties, it should also be acknowledged that serological testing will not capture the full immune risk profile of individuals—most notably, cellular responses, which play an important role in preventing disease and may have a more influential role in immunocompromised patients on selected therapies.8 However, serological testing to assess for a vaccine response would be a pragmatic first screening tool, and would be a step towards providing more tailored care.

As with all pandemic related guidance, adaptations of this proposed strategy would be required as new evidence emerges. Additionally, regardless of specific interventions, or lack thereof in immunocompromised people, it is imperative that the government and other funding bodies commit to ongoing research and surveillance in this population. In the meantime, let us equip immunocompromised people with the information they need to help them live safely with covid-19. Time and time again, they have been left behind by this government's approach to covid-19; they should no longer be denied the freedom to move forward with their lives.} <https://www.bmj.com/content/377/bmj.o966>

**title:** Fit for women: making PPE safe and dignified for women health workers  
  
bmj | 8th april 2022  
  
PPE will not be fit for women unless underlying gender inequities are tackled, say Roopa Dhatt and colleagues

Frontline health workers in all countries have faced exceptional physical and mental challenges responding to the covid-19 pandemic. Many millions have contracted the virus and more than 100 000 health workers have died.1 As 70% of the health workforce, women have been the majority in patient facing roles during the pandemic,2 and are therefore most in need of personal protective equipment (PPE) to protect their health. Yet throughout the pandemic, stories have come from all regions of women working in garbage bags, forced to wear adult diapers, and suffering bruised faces from ill fitting respirators.3 Strikes by health workers in many countries were linked to PPE shortages, including in India where around one million women ASHA (accredited social health activist) community health workers demanded better PPE.4 PPE matters to women. However, there has been little research into the gender differences in PPE needs or effectiveness. In response to the problems raised by women, Women in Global Health undertook research to document and better understand gendered challenges around PPE in the health sector. Common themes emerged from women in different contexts around PPE fit, design, and access.

PPE designed for men. Like many products, PPE is designed on a reference man.6 As a result, the average sizes of PPE are too big for most women. Masks are too big, leaving gaps in the sides, increasing stress and infection risk for women health workers. In the Women in Global Health survey, only 14% of women wore PPE fitted exclusively to them.5 Gowns and other body coverings are not modelled for women’s physique and although PPE may be manufactured in a range of sizes, large will often be the only size procured on the assumption that it will fit. Guidance from the World Health Organization (WHO) on PPE has been notably gender blind, as has donor support for procurement in low and middle income countries.

Women health workers know what they need but their views have not been included in PPE design. Women have also been marginalised in pandemic decision making7 and women’s needs, especially during menstruation, pregnancy, and menopause, have not been accommodated. Women health workers have reported intentionally disrupting their menstrual cycles so that they can cope at work, while pregnant and menopausal women have overheated in unsuitable PPE. Women in Global Health’s research found only around 10% of women health workers could use the bathroom as needed while working, leading to dehydration, infections, and fainting. While many of the gendered issues around PPE are universal, women health workers are not homogenous, and the current “one size fits all” approach to PPE fails to account for diversity, including conventions on hair styling, body and face shapes, and climactic and working conditions. Women from ethnic minorities seem to disproportionately report having PPE that does not fit them. Lack of diversity in PPE design is exacerbated by inequities in access within health systems. Globally, the pandemic has also exposed inequities between countries, especially at the start of 2020 when surging PPE prices hit low and middle income countries particularly hard. The health workers in these countries, the majority of whom were women, have also had least access to covid-19 vaccines.

Change means listening to women. PPE will not be fit for women unless underlying gender inequities in the health workforce are tackled. Women health workers are often clustered into low status jobs and have often been a lower priority for PPE than male colleagues. Although women are the majority of health workers, they hold only 25% of senior leadership roles.2 Women’s anxiety around inadequate PPE is compounded by their “double burden” of care: their common role as the primary care giver within the family means they also have to worry about transmitting covid-19 to family members. Women health workers have considered workplace policies and practices unsafe—for example, the reuse of PPE—but have felt powerless to leverage change. When PPE has not been provided, women health workers have had to buy their own, a last resort that is particularly challenging for women working unpaid or earning less than their male counterparts, especially in low income countries.

Action needed at all levels. New gender responsive standards should be created, and products redesigned so that PPE is fit for women health workers.8 Stronger global governance is required to ensure that the benefits of any innovation in design reach women most in need—for example, unvaccinated community health workers. Innovation in manufacturing is also required: for example, to catalyse more local production of PPE.

Women in Global Health are calling for four actions across the PPE ecosystem. Governments must meet their commitments to protect health workers, including in World Health Assembly Resolutions, by ensuring an adequate supply of PPE and enforcing occupational health law. Employers must meet their duty of care for health workers and should consult women health workers to ensure PPE procurement is needs based. The WHO should strengthen global governance of PPE: for example, by developing “essential” standards for gender responsive PPE for low resource settings, which are similar to the essential medicines list, and by including new gender responsive PPE indicators in pandemic preparedness monitoring. Finally, PPE producers must innovate and tackle gender inequity in PPE, making sure that they include women health workers at the design stage to develop more gender responsive PPE.

Gender equity in leadership in the health sector will enable women to influence the protection of health workers, including through the creation of gender responsive PPE. After two years of the pandemic, women health workers are exhausted, with up to 20% considering leaving the profession.910 Given the serious global shortage of health workers, the world cannot afford to lose one more.  
<https://www.bmj.com/content/377/bmj.o940>

**title:** Covid-19: Ending free testing is a mistake  
  
bmj| 8th april 2022  
  
In light of escalating rates of infection, hospital admissions, and rising sickness absence rates, the UK government should reconsider the end to free covid-19 testing

Helpfully, in the UK, we now have nine more “official” symptoms to consider when deciding if we might have covid-19. What we do not have is universally free testing so many people are left to make up their own minds about whether they have a cold, hay fever, normal aches and pains, or indeed covid-19. If they can afford to, and can find stocks, they can buy a lateral flow test. On the day that free testing finished, we saw one of the highest infection rates of the pandemic so far, with one in 13 of us infected with covid-19.1 We have now got the highest number of people with covid-19 being admitted to hospital, each week, since the pandemic began, and covid-19-related deaths reaching a level not seen for a while. The UK government’s strategy for “Living with covid-19” clearly means potentially living with chaos. This chaos is typified by the woeful communications that surround the government’s decisions. How will this new state of being affect the public, NHS staff, and those who are clinically extremely vulnerable—and what should be done about it?

Firstly, we would urge the government to reconsider the issue of free testing. Over the past two years, families have been used to taking a lateral flow, then following it up with a PCR, and then making sensible decisions about isolation as a result. With a positive test, people have been able to tell their employers that they have covid, and where possible, access sickness payments as a result. For anyone on a low income, and for those who have been hit by the increased cost of living, higher energy bills, and higher fuel costs, asking them to pay for something so important—that a week ago was free—is unreasonable.

Now we have a situation where—without official proof of covid-19—infected people are in work, in schools, in hospitals, and in pubs, shops, and cafes. They are at work because they are worried that if they do not go, they will not be paid and so they are risking the health of those around them because the government says it is fine so to do.

Secondly, we need specific support for those who are clinically extremely vulnerable. In my work as a consultant neurologist, I speak to patients with multiple sclerosis. Before testing ended, they were told that it was crucial to start on antiviral medication within five days of a positive test. In fact, the system worked so well locally that as soon as a positive test was registered, the pharmacy would distribute the medication so that it could be started. Now the entire testing system is being dismantled, that important window of five days is impossible to achieve, leaving immunosuppressed patients at real risk of becoming very ill with longer-term, and lasting effects. Does the government have any answer to this? Where can my patients get their tests from to save their lives?

Finally, at a time when the NHS is on its knees with the backlog and the waiting lists, we are continuing to put staff at risk of becoming infected every time they go to work. Yes, testing is freely available to them, but if patients cannot easily or freely check whether their myriad symptoms might be covid-19, staff are going to be exposed every minute of every day. If those staff then test positive, they will need to stay off and we are back into too many patients, too few staff once again.

Throughout the pandemic the BMA has campaigned for better protection for healthcare workers, but now we are also calling for better protection for everyone. The escalating rates of infection, people needing hospital care and the rising sickness absence rates show that ending free testing is a huge mistake. It needs to be in place to help save lives, and save the NHS, at a time when it needs every bit of help available to it.  
<https://www.bmj.com/content/377/bmj.o936>

**title:** If we are no longer “following the science,” what are we following?  
  
bmj | 7th april 2022  
  
British ministers have now abandoned any pretence that they are “following the science” on covid-19. In their minutes from 10 February 2022, the Scientific Advisory Group for Emergencies (SAGE) warned against removing access to free testing as it would make it harder for people to take precautionary measures and increase anxiety among those who are clinically vulnerable.1 A consensus statement from SAGE’s modelling group, SPI-M, from 2 February, considered that, “a sudden change, such as an end to testing and isolation, has the scope to lead to a return to rapid epidemic growth.”2 And even before these changes are implemented, cases of covid-19 have been rising steeply, with the most recent data from the Office for National Statistics—which along with the now discontinued REACT study is considered the best source of data on the course of the pandemic—estimating that one in every 16 people in England had covid-19 in mid March.3

This poses a challenge for those of us who have been researching the pandemic and who are often asked to comment on government policies. It is impossible to reconcile what is happening with the information we have on health. As Rachel Clarke described recently, frontline NHS staff, some of the heroes of the pandemic, are struggling.4 Some are leaving the health service prematurely, others are burned out, and many have been severely traumatised by their experiences. Data from death certificates, which capture people dying from rather than with covid-19, are running at over 1,000 per week, far higher than at the end of the first and second waves.5 Hospitals in some parts of the country are barely coping.6 The situation is no better in the education sector. Schools have been facing unsustainably high levels of staff absences and over 200 000 children were off sick each day in mid March.7 And those looking for a holiday abroad over Easter are faced with flight cancellations because so many transport workers have covid-19.8 Faced with this seemingly irreconcilable paradox of abandoning covid-19 precautions while so many sectors are struggling, the temptation is to resort to the usual excuse when politicians do things that seem inexplicable. Worried that we should not be straying into politics, we say that politicians have to balance the scientific advice with other considerations brought to their attention. And there we leave it.

This is not an acceptable answer. Independent SAGE was created in response to the lack of transparency about the scientific advice that was being used to inform government policies.9 Almost immediately afterwards, the previously secret membership of SAGE was announced (albeit with a few names withheld). SAGE’s minutes also began to be published. It became possible for anyone to see whether ministers were following the scientific advice they were receiving. But can we see the other advice they are now acting on?

We can of course speculate as to the other factors, but we may struggle to make sense of them. It could be the cost of existing precautions. No one can deny that the pandemic has been expensive, but if this was the main consideration, then surely the government would sort out its procurement systems, which have wasted vast sums of money on personal protective equipment (PPE) that is unusable or do more to recover the vast sums fraudulently obtained in business loans.1011 Or is it the impact on the broader economy? The United Kingdom experienced a massive economic decline during the pandemic, far greater than other industrialised countries. But those other countries are now recovering rapidly while Brexit Britain lags behind.12 Here too, there is an obvious answer, even if it is one that neither the government or the Labour Party is willing to discuss. Or is it some broader measure of wellbeing in the population, however defined? If that was the case, then we might have expected the chancellor, Rishi Sunak, to have used his Spring Statement to offer some hope to those facing the largest hit to their cost of living in a generation.

Faced with these apparent contradictions, we must look to other possible explanations. To take one example, the Conservative Party is increasingly fragmented, with parties within the party. We have the COVID Recovery Group, which emerged from the European Research Group, and the Net Zero Scrutiny Group. We have a prime minister who, so very recently, seemed in peril from his MPs over the Partygate scandal, and who may be again when the long delayed Sue Gray report finally emerges.13 In these circumstances he must be acutely aware of the pressures from his own MPs.

It is entirely reasonable that a prime minister would take account of whether he has support from his back benches. However, if this is indeed the reason for the government’s current policy on covid-19, then we should be told, so that we can discuss its merits or otherwise. The alternative of saying things that are so at odds with the reality we are experiencing simply undermines the trust that is so essential when managing any threat to public health.

A public health perspective recognises that there are many determinants of health, in the scientific and social realms, but also the commercial and political. We are perfectly capable of assessing the wider social, political, and economic arguments for one policy or another. And if we are doing our job properly, we will study all issues that influence our health, from the changing biology of the virus to the political considerations that shape the responses to it. What is not acceptable is that we simply allow politicians to decide which causes of health and disease are “political” and let them decide what is off limits to us.  
<https://www.bmj.com/content/377/bmj.o930>

**title:** COVID-19 vaccination and HIV-1 acquisition  
  
the lancet| 9th april 2022  
  
Susan P Buchbinder and colleagues1 express concern that COVID-19 vaccines utilising replication-defective adenovirus vectors of human serotype 5 (HAdV-5) might increase the risk of HIV-1 acquisition. Such concern has prompted hesitancy to deploy available, safe, and efficacious adenovirus-based COVID-19 vaccines in countries with high HIV-1 incidence…

…Due vigilance and monitoring of adverse events, including HIV-1 infection rates, are absolutely crucial in the pandemic response and the roll-out of vaccines, but still, we would urge global health authorities to license and distribute any efficacious and safe vaccines that are available especially while access to COVID-19 vaccines in low-income countries remains insufficient.  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00332-4/fulltext>

**title:** SARS-CoV-2 nucleic acid testing is China's key pillar of COVID-19 containment  
  
THE LANCET| 7th april 2022  
  
WHO states that timely and accurate diagnostic testing is an essential tool in preventing and controlling the spread of COVID-19.1

With a huge and densely distributed population, China developed a national SARS-CoV-2 nucleic acid testing strategy that has had a pivotal role in containing COVID-19. This strategy involved border entry screening, inpatient screening, rapid screening in fever clinics, and mass screening of the population in an epidemic area.2

China began developing SARS-CoV-2 nucleic acid detection kits soon after the initial outbreak of COVID-19 in Wuhan at the end of 2019. By Jan 31, 2020, the National Medical Products Administration urgently approved six nucleic acid detection kits, and post-market evaluation with a multicentre clinical trial was completed by professional institutions by the end of February, 2020. The sensitivity of these kits was 55·3–95·7%, the specificity above 98% (unpublished)…  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00577-3/fulltext>

**title:** Risk of strong antibody decline in dialysis and transplant patients after SARS-CoV-2mRNA vaccination: Six months data from the observational Dia-Vacc study  
  
THE LANCET regional health - europe| 11th april 2022  
  
Background. Vulnerable dialysis and kidney transplant patients show impaired seroconversion rates compared to medical personnel eight weeks after SARS-CoV-2mRNA vaccination.

Methods. We evaluated six months follow up data in our observational Dia-Vacc study exploring specific cellular (interferon-γ release assay) or/and humoral immune responses after 2x SARS-CoV-2mRNA vaccination in 1205 participants including medical personnel (125 MP), dialysis patients (970 DP) and kidney transplant recipients (110 KTR) with seroconversion (de novo IgA or IgG antibody positivity by ELISA) after eight weeks.

Findings. Six months after vaccination, seroconversion remained positive in 98% of MP, but 91%/87% of DP/KTR (p = 0·005), respectively. Receptor binding domain-IgG (RBD-IgG) antibodies were positive in 98% of MP, but only 68%/57% of DP/KTR (p < 0·001), respectively. Compared to MP, DP and KTR were at risk for a strong IgG or RBD-IgG decline (p < 0·001). Within the DP but not KTR group male gender, peritoneal dialysis, short time on dialysis, BNT162b2mRNA vaccine, immunosuppressive drug use and diabetes mellitus were independent risk factors for a strong decline of IgG or RBD antibodies. The percentage of cellular immunity decline was similar in all groups.

Interpretation. Both vulnerable DP and KTR groups are at risk for a strong decline for IgG and RBD antibodies. In KTR, antibody titres peak at a markedly lower level and accelerated antibody decline is mixed with a delayed/increasing IgG, RBD-IgG, or cellular immune response in a 16% fraction of patients. In both populations, immune monitoring should be used for early timing of additional booster vaccinations.  
<https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00064-3/fulltext>

**title:** The epidemiological relevance of the COVID-19-vaccinated population is decreasing after booster vaccination, as shown by incidence rate ratios [correspondence]

the lancet regional health - europe| 11th april 2022  
  
The World Health Organization has suspended the supply of Covaxin through UN procurement   
Kampf1,2 describes an increase in symptomatic COVID-19 cases among fully vaccinated people and raises two central concerns: first, that “many decisionmakers” ignore the vaccinated as a transmission source and, second, that this ignorance leads to “inappropriate stigmatisation of unvaccinated people”.

To illustrate this, he presents reports describing a high proportion of breakthrough infections among the vaccinated.1,2 Moreover, he depicts Robert Koch-Institute (RKI) data (21 July–27 October 2021), demonstrating a constant rise in the proportion of the vaccinated among symptomatic COVID-19 cases, until a maximum of 58.9% was reached.3 However, omission of some very critical information provides a distorted view…  
<https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00065-5/fulltext>

**title:** Dosing interval strategies for two-dose COVID-19 vaccination in 13 middle-income countries of Europe: Health impact modelling and benefit-risk analysis  
  
the lancet regional health - europe| 11th april 2022  
  
Background. In settings where the COVID-19 vaccine supply is constrained, extending the intervals between the first and second doses of the COVID-19 vaccine may allow more people receive their first doses earlier. Our aim is to estimate the health impact of COVID-19 vaccination alongside benefit-risk assessment of different dosing intervals in 13 middle-income countries (MICs) of Europe.

Methods. We fitted a dynamic transmission model to country-level daily reported COVID-19 mortality in 13 MICs in Europe (Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Bulgaria, Georgia, Republic of Moldova, Russian Federation, Serbia, North Macedonia, Turkey, and Ukraine). A vaccine product with characteristics similar to those of the Oxford/AstraZeneca COVID-19 (AZD1222) vaccine was used in the base case scenario and was complemented by sensitivity analyses around efficacies similar to other COVID-19 vaccines. Both fixed dosing intervals at 4, 8, 12, 16, and 20 weeks and dose-specific intervals that prioritise specific doses for certain age groups were tested. Optimal intervals minimise COVID-19 mortality between March 2021 and December 2022. We incorporated the emergence of variants of concern (VOCs) into the model and conducted a benefit-risk assessment to quantify the tradeoff between health benefits versus adverse events following immunisation.

Findings. In all countries modelled, optimal strategies are those that prioritise the first doses among older adults (60+ years) or adults (20+ years), which lead to dosing intervals longer than six months. In comparison, a four-week fixed dosing interval may incur 10.1% [range: 4.3% - 19.0%; n = 13 (countries)] more deaths. The rapid waning of the immunity induced by the first dose (i.e. with means ranging 60-120 days as opposed to 360 days in the base case) resulted in shorter optimal dosing intervals of 8-20 weeks. Benefit-risk ratios were the highest for fixed dosing intervals of 8-12 weeks.

Interpretation. We infer that longer dosing intervals of over six months could reduce COVID-19 mortality in MICs of Europe. Certain parameters, such as rapid waning of first-dose induced immunity and increased immune escape through the emergence of VOCs, could significantly shorten the optimal dosing intervals.  
<https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00074-6/fulltext>

**title:** Fourth Dose of BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting

new england journal of medicine| 13th april 2022  
  
BACKGROUND. With large waves of infection driven by the B.1.1.529 (omicron) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), alongside evidence of waning immunity after the booster dose of coronavirus disease 2019 (Covid-19) vaccine, several countries have begun giving at-risk persons a fourth vaccine dose.

METHODS. To evaluate the early effectiveness of a fourth dose of the BNT162b2 vaccine for the prevention of Covid-19–related outcomes, we analyzed data recorded by the largest health care organization in Israel from January 3 to February 18, 2022. We evaluated the relative effectiveness of a fourth vaccine dose as compared with that of a third dose given at least 4 months earlier among persons 60 years of age or older. We compared outcomes in persons who had received a fourth dose with those in persons who had not, individually matching persons from these two groups with respect to multiple sociodemographic and clinical variables. A sensitivity analysis was performed with the use of parametric Poisson regression.

RESULTS. The primary analysis included 182,122 matched pairs. Relative vaccine effectiveness in days 7 to 30 after the fourth dose was estimated to be 45% (95% confidence interval [CI], 44 to 47) against polymerase-chain-reaction–confirmed SARS-CoV-2 infection, 55% (95% CI, 53 to 58) against symptomatic Covid-19, 68% (95% CI, 59 to 74) against Covid-19–related hospitalization, 62% (95% CI, 50 to 74) against severe Covid-19, and 74% (95% CI, 50 to 90) against Covid-19–related death. The corresponding estimates in days 14 to 30 after the fourth dose were 52% (95% CI, 49 to 54), 61% (95% CI, 58 to 64), 72% (95% CI, 63 to 79), 64% (95% CI, 48 to 77), and 76% (95% CI, 48 to 91). In days 7 to 30 after a fourth vaccine dose, the difference in the absolute risk (three doses vs. four doses) was 180.1 cases per 100,000 persons (95% CI, 142.8 to 211.9) for Covid-19–related hospitalization and 68.8 cases per 100,000 persons (95% CI, 48.5 to 91.9) for severe Covid-19. In sensitivity analyses, estimates of relative effectiveness against documented infection were similar to those in the primary analysis.

CONCLUSIONS. A fourth dose of the BNT162b2 vaccine was effective in reducing the short-term risk of Covid-19–related outcomes among persons who had received a third dose at least 4 months earlier.  
<https://www.nejm.org/doi/full/10.1056/NEJMoa2201688?query=featured_coronavirus>

**title:** Myocarditis Adverse Event Less Common After COVID-19 Vaccine Booster

JAMA| 12th april 2022  
  
Data are needed regarding the effectiveness of a third dose of a messenger RNA (mRNA) vaccine   
he risk of adolescents developing myocarditis is lower after a booster dose of the BNT162b2 (Pfizer-BioNTech) COVID-19 vaccine than after the second dose, according to a CDC analysis of data from the Vaccine Adverse Event Reporting System (VAERS).

Myocarditis is a rare but serious adverse event associated with COVID-19 mRNA vaccination. To assess whether this adverse event was also associated with booster doses administered to adolescents, the authors analyzed reports submitted to the VAERS system and v-safe between December 9, 2021, and February 20, 2022.

During the study period, roughly 2.8 million US adolescents received a BNT162b2 booster dose. About 92% of the 914 reports submitted to VAERS were not serious. Improper vaccine storage, dizziness, and fainting were the most common nonserious events.

Serious reports included 64 myocarditis cases. Provider interviews and chart reviews confirmed that 32 of these cases—all of which occurred among boys—met the CDC’s myocarditis definition. Of the confirmed cases, 27 patients required hospitalization, but all were discharged and had recovered or were recovering. The confirmed myocarditis rate after a booster dose was 11.4 per 1 million administered doses among adolescent boys aged 12 to 17 years. By comparison, the myocarditis rate after the second dose in the primary vaccine series was 70.7 per 1 million among 12- to 15-year-olds and 105.9 per 1 million doses among 16- to 17-year-olds.

V-safe, a voluntary smartphone-based system created by the CDC to monitor post–COVID-19 vaccination symptoms, collected data from 3418 adolescents who received a BNT162b2 booster dose. About 80% reported a local or systemic reaction, most commonly injection site pain, fatigue, headache, and muscle pain. The authors noted that clinicians, parents, and adolescents should be aware that reactions are common after receiving a booster dose but that serious adverse events are rare.  
<https://jamanetwork.com/journals/jama/fullarticle/2790928>

**title:** Vaccine Booster Dose Appears to Reduce Omicron Hospitalizations

JAMA | 12th april 2022  
  
On January 2, 2022, Israel began administering a fourth dose of BNT162b2 vaccine to persons 60   
The COVID-19 mRNA vaccines’ 2-dose primary series appeared to provide less protection against hospitalization from Omicron variant infections than Alpha and Delta infections, according to a recent study. A booster dose, however, was associated with increased effectiveness against Omicron hospitalizations at the same high levels achieved against earlier variants with 2 doses.

The study included data from 11 690 adults admitted to 21 US hospitals from March 11, 2021, to January 14, 2022, about half of whom had laboratory-confirmed COVID-19. The other half served as a control group. To calculate vaccine effectiveness, researchers compared the odds of vaccination between the 2 groups. In the COVID-19 group, SARS-CoV-2 variants were determined using whole-genome sequencing or were classified based on the predominant variant at the time of hospitalization. Sequencing results were available for 45.4% of the 5728 SARS-CoV-2 infections…  
<https://jamanetwork.com/journals/jama/fullarticle/2790956>

**title:** Large US Study Examines First 6 Months of COVID-19 Vaccine Safety Data

jama | 12th april 2022  
  
During the first 6 months of the US COVID-19 vaccination campaign, most adverse events reported to surveillance systems were mild and short-lived, researchers from the Centers for Disease Control and Prevention reported in The Lancet Infectious Diseases. The study examined safety data collected through the new v-safe surveillance system and the Vaccine Adverse Event Reporting System (VAERS).

Nearly 300 million mRNA vaccine doses were administered in the US between December 14, 2020, and June 14, 2021, of which about 167 million were BNT162b2 (Pfizer-BioNTech) and 132 million were mRNA-1273 (Moderna).

The VAERS received 340 522 reports during this time: 92.1% were classified as nonserious; 6.6% as serious, not resulting in death; and 1.3% were deaths. The most common serious reports aside from deaths were shortness of breath, fever, fatigue, and headache.

COVID-19 vaccines were administered under Emergency Use Authorization (EUA) during the study period, and providers were required to report all serious postvaccination adverse events, including deaths, even if they were unlikely to have been associated with vaccination. The most common causes of death were heart disease and COVID-19, according to death certificates and autopsy reports that were available for about 18% of 4471 deaths. The authors noted that they “found no unusual patterns in cause of death among the death reports received.”

For v-safe participants, transient reactions were more common after mRNA-1273 than BNT162b2 and were more frequent after the second dose than the first dose of either vaccine. Following their second dose, about 21% of v-safe participants who received BNT162b2 and about 33% of those who received mRNA-1273 reported they were unable to do normal activities. There were more reports of reactions and health effects involving females and people younger than 65 years than males and older people.

The researchers concluded that the findings from both surveillance systems were consistent with the pre-EUA vaccine clinical trials.  
<https://jamanetwork.com/journals/jama/fullarticle/2790957>

**title:** Immunogenicity and Risk Factors Associated With Poor Humoral Immune Response of SARS-CoV-2 Vaccines in Recipients of Solid Organ Transplant: A Systematic Review and Meta-Analysis

jama network open| 12th april 2022  
  
Question What are the humoral immune response rates and risk factors associated with diminished response after COVID-19 vaccination in recipients of solid organ transplant?

Findings In this systematic review and meta-analysis of 29 studies and 11 713 recipients of solid organ transplant, seroconversion rates increased with progressively increased numbers of mRNA COVID-19 vaccine doses. Older age, recent transplantation, deceased donor status, active use of antimetabolites, and recent exposure to antithymocyte globulin or rituximab were risk factors associated with diminished humoral immune response after receiving 2 doses of mRNA vaccines.

Meaning These findings suggest that more efforts are needed to modulate the risk factors associated with reduced humoral responses among recipients of solid organ transplant.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790991>

**title:** Suboptimal Antispike Antibody Levels Following Vaccination in Recipients of Solid Organ Transplant—Variance of Concern

jama network open | 12th april 2022  
  
Immunity developed through vaccination has been shown to be protective against hospitalization and death from SARS-CoV-2 in the general population.1 Initial clinical trials of SARS-CoV-2 vaccines excluded participants who were immunocompromised, including recipients of solid organ transplant (SOT), who are considered at high risk of SARS-CoV-2 infection and may have a risk of mortality of 20% with natural infection.2,3 Compared with the general population, recipients of SOT had a higher risk of breakthrough infection and associated hospitalization and death.4 It is recognized that many individuals who are immunocompromised may not achieve antispike antibody seroconversion despite vaccination, and the study by Manothummetha et al3 is a timely systematic review and meta-analysis of the humoral responses in recipients of SOT after SARS-CoV-2 vaccination…  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2790995>

**long-term effects**

**title:** Long COVID: the elephant in the room

the lancet diabetes & endocrinology| 7th april 2022  
  
On April 1, 2022, the UK government ended free universal COVID-19 testing, as part of the Living with COVID-19 plan. The legal requirement to isolate if positive has also been scrapped in England under this plan, and all other public health restrictions have now been removed.

The Living with COVID-19 strategy portrays the restrictions from the past 2 years as “necessary” but as also coming with a “huge toll on wellbeing and economic output”, and states that the “next phase of the COVID-19 response is to enable the country to manage COVID-19 like other respiratory illnesses, while minimising mortality and retaining the ability to respond if a new variant emerges with more dangerous properties than the Omicron variant”.

At a time when SARS-CoV-2 infections remain at record levels in the UK due to the omicron (B.1.1.529) sublineage variant BA.2 (about one in 13 people were estimated to be infected in the week ending March 26, 2022), and hospitalisation and mortality rates are rising again, removal of all public health restrictions is problematic, if not highly unethical. The new policies will also disproportionally affect the clinically vulnerable and those who are in situations of precarious employment, further increasing disparities. Adding to this exceptionally bleak picture, there is now irrefutable evidence pointing to a high incidence and large burden of long COVID, with devastating effects on quality of life and on the economy already visible. As of Jan 31, 2022, according to data from the Office for National Statistics, 1·5 million people in the UK (2·4% of the population) reported experiencing long COVID symptoms, with 65% of those reporting a negative impact on their day-to-day activities. In the USA and UK, millions are taking long-term absence from the workforce due to long COVID.

The adverse health effects from long COVID range from fatigue and difficulty concentrating, to neurological and neuropsychiatric symptoms, respiratory and cardiovascular problems, and metabolic disease. Earlier in the pandemic, the discourse largely centred on acute illness, and perhaps rightly so. However, long COVID has now clearly emerged as a public health concern that will not only disrupt health care of people living with non-communicable diseases (NCDs) but likely also increase the burden of NCDs.

The Lancet Diabetes & Endocrinology has, on many occasions, editorialised on the alarming increasing rates of poor metabolic health worldwide, and, in August, 2020, we published a large population study showing increased risk of death from COVID-19 in people with type 1 and type 2 diabetes. In this issue of the journal, Yan Xie and Ziyad Al-Aly report significantly increased risk of diabetes in the post-acute phase (>30 days) of COVID-19 in a cohort of US veterans, including those who had had mild infections and for whom no previous risk factors for diabetes were known. Publication of this study follows the release of data from the US Centre for Disease Control and Prevention showing that people younger than 18 years were more likely to receive a new diabetes diagnosis in the post-acute phase of COVID-19 than those without it or with pre-pandemic respiratory infections. However, a number of other studies did not report similar associations. A cohort from Scotland shared on the preprint server medRxiv, found that incidence of type 1 diabetes in children (aged 0–14 years) during 2020–21 was 20% higher than the 7-year average, but these findings were attributed to other causes and not a direct effect of SARS-CoV-2.

Large and well controlled epidemiological studies with reasonably long follow-up (>1 year) will be key to further clarify the association between COVID-19, new-onset diabetes, and metabolic complications, and assess potential causal relationships. Epidemiological efforts should also be examined in the context of comprehensive clinical data, such as data from CoviDIAB, a global clinical registry launched in June, 2020, to determine the presentation and course of COVID-19–related diabetes. The contributions of basic and translational research to our understanding of COVID-19 and its prevention have been remarkable and should continue to complement and inform clinical research. Selfless and open collaboration within the international scientific community will be fundamental. If the link between COVID-19 and new-onset diabetes holds true, even a small increase in the global prevalence of diabetes could have disastrous consequences.

In a world where the new mantra is to learn to live with COVID-19, long COVID cannot be ignored. Any strategy to learn to live with COVID-19 must also aim for a fair, thriving, and healthy post-pandemic world—that is what return to normalcy should look like.  
<https://www.thelancet.com/journals/landia/article/PIIS2213-8587(22)00111-5/fulltext>

**title:** Olfactory Impairment and Mortality—Is Smell Loss Deadly?

jama otolaryngology| 7th april 2022  
  
The COVID-19 pandemic has elevated the world’s attention to olfactory impairment (OI). As a cardinal symptom of the many early variants of the SARS-CoV-2 virus, we have never seen such global attention toward one of our most important senses. Although the prevalence of OI has increased dramatically with COVID-19, OIs have long been a significant health concern. Prior to the COVID-19 pandemic, the median length of time from onset of OI to evaluation by a clinician was 13 months, with many individuals waiting up to 3 years before seeking evaluation. During that time, patients did not receive treatment or counseling, compounding the potential associations of OI with patient health…  
<https://jamanetwork.com/journals/jamaotolaryngology/article-abstract/2790857>

**title:** Biden Administration Outlines Strategy to Tackle Long COVID  
  
JAMA | 12th april 2022  
  
In a presidential memorandum issued last week, the Biden administration ordered the secretary of Health and Human Services (HHS) to create a national action plan to coordinate research on long-term effects of COVID-19, or long COVID, and support for patients experiencing the condition.  
  
The HHS “will be leading a government-wide response to Long COVID focused on three main goals: improving care services and other support for individuals with Long COVID; enhancing education and outreach among the public-private sector and the medical community; and advancing research to support both goals,” HHS Secretary Xavier Becerra said during a White House COVID-19 Response Team briefing…  
<https://jamanetwork.com/journals/jama-health-forum/fullarticle/2791210>

**workforce well-being**

**title:**  Solving retention after the pandemic—authenticity and flexibility might help

BMJ| 11th april 2022  
  
Over the past two years, the NHS workforce has shown flexibility so that it can deliver safe and consistent clinical practice in the pandemic.1 This has included changing the working environment, working across teams, and working differently, delivering different skill sets to different patient groups. Staff have shown a degree of willingness to make these changes, despite sometimes having to make personal sacrifices.

This prolonged period of uncertainty and challenge will have brought lessons on good and less good practice. Some positive, evidence based changes could be continued, and all parties should be considered in the decision making process. But this is not happening.

Salaried GPs who have worked entirely off site for the past two years using telemedicine technology to successfully deliver timely patient interactions are now expected to fully return on site. Staff who were previously shielding off site but delivering their work outcomes are understandably reluctant to return to work environments with closed ventilation in multi-occupancy offices.

Requests to trial hybrid work options, which balance time off site and on site with colleagues’ work patterns, have been denied. Peers who do not have underlying immunosuppressive disorders are being asked why they should have more flexibility. People risk being perceived as “not team players.” Reasonable adjustments under the Equality Act 2010 are not always fully considered and explored.

Now, we are potentially moving away from the flexible attendance management processes recommended by NHS Employers back to the pre-pandemic operational target driven delivery system. But a phased individualised strategy might be better for all parties.

The NHS People Plan emphasises staff health and wellbeing as important. So being authentic in response to that “promise” might lead to better bilateral respect and improved retention.  
<https://www.bmj.com/content/377/bmj.o891.full>

**title:**  NHS workforce shortages and staff burnout are taking a toll

bmj| 11th april 2022  
  
“We have witnessed senior experienced staff crying with frustration and anger…[they are] mentally drained and despite their best efforts have seen patients suffer and have received negative comments from distraught relatives and carers.”

These are the widely reported words of managers at Royal Preston Hospital in a letter describing how NHS employees are being reduced to tears.1 It’s an eye opening account of what’s happening in our health service.

All across the NHS, widespread workforce shortages and staff burnout are taking their toll on hard working, but overstretched professionals under sustained pressure.

Over the past few weeks, covid-19 infection rates have soared again in England. Hospital admissions and deaths have risen too, although not as high as before thanks to a successful mass covid-19 vaccination by the NHS. There has been a worrying increase in the number of NHS staff off work due to covid-19 which is having a knock-on effect on patient care, on efforts to deal with care backlogs, and on meeting ongoing demand for services.

The last two years have undoubtedly been the most challenging period in NHS’s history. Staff continue to work flat out, doing their best for patients, but many of the problems we face now existed long before the pandemic and won’t disappear overnight. There are currently 110 000 job vacancies across NHS trusts and many thousands more in primary care.

The whole NHS wants to get back to pre-pandemic levels of activity as soon as possible, but some necessary infection control measures must remain while covid-19 cases stay high to protect vulnerable patients, constraining how quickly we can deal with the backlogs.

At the same time, NHS trust leaders are doing their bit to ease the strain on the public purse, working hard to find more efficiencies, cut costs, and find the £330million savings asked of them. That’s an increasingly tough task as inflation and the cost of energy and fuel soar.

Staff satisfaction with pay is at its lowest in five years too. In the face of the mounting cost of living crisis, staff must see a meaningful pay rise from the government this year. As collective employers of 1.4 million people, trust leaders know the spiralling day-to-day costs which their workers face and worry about the impact on younger and lower paid staff.

It's no surprise that all of this has dented morale and wellbeing, reflected in the results of the latest NHS staff survey.2 Barely one in four (27 per cent) people working in the NHS feel that there are enough staff in their organisation to allow them to do their jobs properly, while there are also concerning increases in the proportion of staff suffering work related stress and, sadly, thinking about quitting the NHS.

Trust leaders take the effect of workforce pressures on their people and services extremely seriously. Almost all respondents who replied to a recent NHS Providers survey said that staff shortages are having a serious and detrimental impact on services and will hinder efforts to deal with those major care backlogs. Trusts are doing all they can to tackle the situation but need more staff to be able to reduce delays and to treat patients as quickly as possible.

It’s tough too to see a sharp drop in public satisfaction with the NHS, although given the impact of the pandemic it isn’t completely surprising.3 We want the public and politicians to understand the pressures which the whole of our health service is under, with huge strain on exhausted staff. They need to see that the government will offer support to help boost morale and retention.

NHS Providers, along with more than a hundred health and social care organisations, have supported the inclusion of measures in the Health and Care Bill going through parliament requiring ministers to publish regular independent assessments of the number of health and care workers needed to make workloads sustainable. This has so far been resisted by the government.

As workers and employers start paying for the welcome extra investment from the Health and Care Levy it’s vital too that the government comes up with a fully costed and funded long term plan to ensure that we have the workforce we need to meet increased demand for NHS and social care services today and in the future.  
<https://www.bmj.com/content/377/bmj.o945>

**title:**  Tracking Turnover Among Health Care Workers During the COVID-19 Pandemic: A Cross-sectional Study

jama health forum| 8th april 2022  
  
Question Which health care workers were at highest risk of leaving the workforce during the COVID-19 pandemic compared with prepandemic levels?

Findings This observational cross-sectional study among 125 717 health care workers found that long-term care workers and physicians saw an upward trend in turnover rates. Health care workers employed as health aides and assistants, those of historically marginalized racial and ethnic groups, and those with young children, particularly women, had persistently high turnover rates and were experiencing a slow recovery.

Meaning These findings suggest that turnover rates are returning to prepandemic levels across most groups of health care workers, yet the recovery is uneven; targeted solutions are needed to ensure an adequate health care workforce is available to meet patient demand.  
<https://jamanetwork.com/journals/jama-health-forum/fullarticle/2790961>

**HEALTH MANGEMENT & recovery**

**title:** Covid-19: Hospital and ambulance services struggle with huge demand and staff illness

BMJ | 11th april 2022  
  
Hospitals and ambulance services in England are facing “extreme pressures” and a high volume of staff absences, forcing some to declare critical incidents and others to warn of 12 hour waits for patients in hospital emergency departments.

Portsmouth’s Queen Alexandra Hospital and South Central Ambulance Service both declared critical incidents on 6 April, with the hospital warning, “Our beds are full and our emergency department remains full with patients requiring admission . . . We are only able to treat patients with life threatening conditions and injuries.”1 The ambulance service reported a “large volume of calls being received throughout the day and into the night and increased challenges in releasing some of our ambulances from busy acute hospitals.”

The pressure is not just being felt in southern England. In the north, where covid cases are rising, hospital trusts across West Yorkshire and Harrogate have warned of waits of up to 12 hours in emergency departments. On 5 April the West Yorkshire Association of Acute Trusts, which encompasses six hospital trusts, reported a 14.2% higher number of attendances than in the same week in 2021.

With emergency departments around the country inundated, ambulances have been increasingly delayed. In the week ending 3 April 26.9% of arrivals were delayed more than 30 minutes, the worst performance on record. The previous record was just over 18% in the week ending 6 January 2019.

In the week to 6 April an average of 71 088 staff in acute care trusts in England were absent each day because of sickness. Of these absences, 40% were related to covid, and this proportion was even higher in the South West (52% in the week to 3 April).

On top of staff shortages, hospitals are struggling to discharge patients. The number of patients staying in acute care despite no longer meeting the criteria rose to just under 13 000 in the week to 3 April, the highest so far this winter.

The NHS Confederation’s director of policy, Layla McCay, said, “This pandemic is not yet over, despite government rhetoric.” She added, “The government must be honest with the public about the need for people to take steps to curb the spread of covid where it is possible for them to do so. The government must also be honest about what people can expect from the NHS during this period of incredible strain.”

Have infections peaked? The latest Office for National Statistics data show that in England the number of people testing positive for SARS-CoV-2 has remained high, with around one in 13 estimated to have had the virus during the week ending 2 April. ONS found that although the percentage of people testing positive had fallen in the South East, increases were seen in the East Midlands, North East, North West, and Yorkshire and the Humber.

In Wales, infections have increased from one in 14 in the previous week (ending 26 March) to around one in 13. But Scotland saw a decrease from one in 12 to one in 13 over the same period, and in Northern Ireland there may also have been a decrease, from one in 15 to one in 16, although ONS noted this trend was uncertain.

Sarah Crofts, head of analytical outputs for the ONS’s Covid-19 Infection Survey, said, “While infections remain high, there are early signs in our latest data that they may no longer be increasing in some parts of the UK. It is too early to say if infections have peaked in England and Scotland. We will continue to monitor the data closely.”  
<https://www.bmj.com/content/377/bmj.o950>

**title:** COVID-19 Vaccine Refusal and Fair Allocation of Scarce Medical

new england journal of medicine | 8th april 2022

When hospitals face surges of patients with COVID-19, fair allocation of scarce medical resources remains a challenge. Scarcity has at times encompassed not only hospital and intensive care unit beds—often reflecting staffing shortages—but also therapies and intensive treatments. Safe, highly effective COVID-19 vaccines have been free and widely available since mid-2021, yet many Americans remain unvaccinated by choice. Should their decision to forgo vaccination be considered when allocating scarce resources? Some have suggested it should,1 while others disagree. We offer a framework for evaluating when it is ethical and briefly discuss its legality in American law…  
<https://jamanetwork.com/journals/jama-health-forum/fullarticle/2790959>

**title:** Hidden Waits: The Lasting Impact Of The Pandemic On Children’s Services In The Community

nhs confederation| 11th april 2022  
  
The number of UK patients self-funding their own hip and knee operations has risen substantially   
This briefing brings together new evidence about backlogs and increasing demand for children and young people's services. It also demonstrates what community providers are currently doing to meet demand, including how they are innovating, and makes a series of recommendations on the national support needed, both now and in the longer term…  
<https://kingsfund.blogs.com/health_management/2022/04/hidden-waits-the-lasting-impact-of-the-pandemic-on-childrens-services-in-the-community.html>

**public health & health inequalities**

**title:** The Tobacco Wars’ Lessons for the Vaccination Wars

new england journal of medicine | 13th april 2022  
  
Covid-19 will soon have killed 1 million Americans. When vaccines first became available in late 2020, surveys indicated that about one third of U.S. adults were keen to be vaccinated, 15% expressed strong resistance to vaccination (a proportion that has stayed fairly constant), and the remainder didn’t harbor strong ideological resistance.1 About 27% of U.S. adults remain unvaccinated.1 An important challenge involves reaching the undecided — an issue for booster doses, future pandemics, and all vaccines. In the midst of deafening noise, much of it hateful, filled with falsehoods, and purely political, we believe public health shouldn’t lose its voice.

Lessons from the tobacco wars can provide perspective. In the case of tobacco, preventable deaths were fueled by an industry that influenced millions of people with messages suggesting that using its products was glamorous and normal. Nearly half of U.S. adults smoked cigarettes in the 1960s.2 The current rate of about 12.5% reflects decades of multifaceted public health efforts to deglamorize and denormalize tobacco use and make it less socially acceptable. The science of tobacco’s harms was initially summarized in the first U.S. Surgeon General’s report on smoking and health in 1964; the tobacco industry attacked the data, and the report’s effects were minimal. C. Everett Koop’s 1986 report, a massive compilation of epidemiologic and biologic data, overwhelmingly established tobacco use as a major preventable cause of cancer and death and, most importantly, highlighted the harm associated with involuntary smoking.

Koop and others were vilified by the tobacco industry, which mounted a sustained campaign that aggressively raised doubts about this science, publicized misinformation about smoking, emphasized tobacco’s economic importance, and warned against restricting individual freedom. Industry leaders lied to Congress and the public about their long-standing knowledge that nicotine was addictive and that tobacco use could be lethal. Although the initial debate over tobacco control was focused on individual choice, two 1981 studies changed the conversation by documenting that nonsmoking wives of smokers had a higher risk of lung cancer than nonsmoking wives of nonsmokers. At least a dozen other studies in the next few years proved the dangers of secondhand smoke. What was initially a concern specific to smokers became everyone’s problem when the public understood that one person’s actions endangered other people’s lives.

Congress has never enacted a federal smoking ban. Efforts of former Food and Drug Administration (FDA) commissioner David Kessler and others to have the FDA restrict nicotine and tobacco products were rejected by the Supreme Court in 2000.3 Congress granted the FDA limited authority to regulate tobacco in 2009, enabling restriction of marketing and sales to youth and requiring warning labels on smokeless tobacco. Nevertheless, broad-based strategies at all levels of society have been important. Cessation messages from health professionals have reached millions of smokers. Policies restrict smoking in public places, workplaces, schools, restaurants, bars, and airplanes. These efforts have made the importance of clean air, not just a reduction in smoking, part of the message behind the goal of broadening the social norm. Also important have been public information messages delivered by athletes, artists, and actors, as well as hard-hitting, sometimes graphic counteradvertising that features smokers debilitated by tobacco use who are expressing regret over smoking and urging others not to start. The Centers for Disease Control and Prevention (CDC) Tips from Former Smokers campaign, which began in 2012 and is still airing on television, has triggered more calls to smoking “quit lines” and led to increased cessation rates. Strategies such as taxation, advertising restrictions on tobacco products, and actions to counter the tobacco industry’s efforts to recruit young people to use its products have contributed to reductions in smoking. Legal battles initiated by state attorneys general, arguing for tobacco companies to be held liable and compensate states for Medicaid costs for people harmed by smoking, resulted in the 1998 Master Settlement Agreement, the largest civil-liability settlement in U.S. history.

Efforts undertaken by the antivaccination movement, which is hardly new but is thriving during the Covid-19 pandemic, bear many similarities to strategies used during the tobacco wars. Although not financed by a single industry, the movement is well supported by certain political figures, physicians, and media companies, and it sows doubt and distrust in science and government. Vast amounts of misinformation about vaccine safety and effectiveness are readily available online. Whereas the tobacco wars initially involved massive advertising and public relations campaigns, social media and right-wing media channels now promote conspiracy theories that vaccines deliver microchips to control behavior, render vaccinees sterile, or harm fetuses. The vilification of scientific leaders such as Anthony Fauci is a replay of attacks on Koop and others. Once again, important decisions affecting the public’s health are being made not by public health experts, but by the courts — including the Supreme Court.

Of course, there are important differences between tobacco control and vaccination; for example, the effects of interventions to prevent smoking initiation and chronic disease often take decades to materialize, whereas vaccinations usually reduce hospitalizations and acute viral illness within days or weeks. CDC data clearly show that approved Covid-19 vaccines have reduced hospitalizations and deaths in the United States, and household-transmission studies have shown that vaccination reduces SARS-CoV-2 transmission.4 Vaccination also prevents indirect harm to the health care system.

We believe it’s necessary to counter misinformation about vaccines with a compelling public information campaign modeled on the successes of the tobacco wars — one that illustrates the harm caused by Covid-19 and the power of vaccines. Getting vaccinated and boosted should be the accepted social norm during a pandemic. An adaptation of the Tips campaign for vaccination could feature many of the real patients in intensive care units who, just before being intubated, express deep regret over failing to get vaccinated. Many of these patients only then request vaccination and are told it’s too late. Unvaccinated people often assume that doctors and hospitals will always be available to them if they get sick. Messages could therefore also feature health care workers attesting to the strain that Covid-19 places on clinicians and on patients requiring treatment for any condition. There is an opportunity to mount a serious effort to provide accurate vaccination information using the same media channels on which people currently consume misinformation.

Vaccine mandates have helped boost vaccination rates in some places by making being vaccinated a social norm, similar to wearing a seat belt and pausing for security checks in airports. Regulations at the local and community levels, such as requiring proof of vaccination to enter public spaces and maintain local business functions, may be even more effective than federal mandates. Liability litigation seeking compensation for harm caused by businesses that don’t require their workers to be vaccinated merits consideration, even though the Supreme Court rejected private-employer vaccine mandates from the Occupational Safety and Health Administration.

Trusted personal physicians remain the best source for the effective transmission of health information. But many people at risk of remaining unvaccinated have had less-than-optimal access to and experiences with the health care system, which has engendered mistrust. Furthermore, despite the extraordinary efforts of most physicians during the pandemic, not all physicians provide truthful information, and states have inadequately regulated the licenses of those who spread harmful misinformation.5

Public health practitioners knew for years that tobacco use causes cancer, but scientific knowledge alone had a minimal effect on smoking behavior. Just as the awareness that smokers endanger others marked a turning point for tobacco control, conveying the message that unvaccinated people endanger their family members, communities, and the health care system may be effective. A well-funded, multifaceted communications effort will again be required to change the behavior of some people who are still undecided.

Freedom of choice remains; people can still smoke cigarettes and decline vaccinations. But the roadmap drawn by tobacco-control efforts shows that the public mindset can be tilted toward public health and social good. With vaccination, this work shouldn’t take decades; it needs to begin immediately.  
<https://www.nejm.org/doi/full/10.1056/NEJMp2202618?query=featured_coronavirus>

**title:** Effect of covid-19 and social on disease burden in the over 70s: we must act soon

bmj | 7th april 2022  
  
Question Was the US Veterans Affairs initiative to distribute video-enabled tablets during COVID-19   
The GBD 2019 Ageing Collaborators analysis of the 2019 study of the global burden of disease and injury in people over 701 will serve to highlight the effects of the past two years of the pandemic.

The State of Ageing 2022 report from the Centre for Ageing shows that men and women now have a lower life expectancy and are living more years of life with disability.2 While this has been attributed to the pandemic, we have to remember that its effects are more complex than simply that of a virus.

For example, studies have shown negative effects on eating habits and weight—with those who are overweight gaining more weight and those who are underweight losing more.34 Other studies point to increased sedentary behaviour and decreased physical activity.5 Specifically within the elderly populations, there were additional challenges: advice to isolate, for example, created increased barriers to normal living that impacted mental and physical health.6

In my role as anticipatory care lead for a London primary care network, I see patients who are still dealing with these effects of the pandemic as part of their daily lives. And while I am not aware of published empirical evidence to support this, in our local area it seems the number of housebound and immobile patients has dramatically increased, while these same patients are suffering decreased access to services as a result of digitalisation and remote working.

My fear is that the next study that investigates the burden of disease in adults over 70 will show a much different picture, and early and concerted action is needed to rectify the situation.  
<https://www.bmj.com/content/377/bmj.o906>

**title:** Association of the COVID-19 Pandemic With Rates of Prostate Cancer Biopsies and Diagnoses in Black vs White US Veteran

jama oncology | 7th april 2022  
  
Question What is the association of the COVID-19 pandemic with prostate biopsy and prostate cancer (PC) diagnosis rates, evaluated by race, in the Veterans Affairs Health Care System?

Findings Among 51 606 included men, the estimated number of missed PC diagnoses from March 2020 through March 2021 ranged from 97 to 573 cases. Prior to the pandemic, biopsy rates were statistically significantly higher among Black vs White men; however, there were no statistically significant changes in biopsy rates associated with race at the onset of the pandemic nor during the recovery period from June 2020 through March 2021, with similar trends observed for PC diagnosis rates.

Meaning These results suggest that prostate biopsy volume and PC diagnosis rates decreased in the Veterans Affairs Health Care System during the COVID-19 pandemic, with no statistically significant changes noted by race.  
<https://jamanetwork.com/journals/jamaoncology/fullarticle/2790999>

**title:** Association of COVID-19 and Endemic Systemic Racism With Postpartum Anxiety and Depression Among Black Birthing Individuals

jama | 13th april 2022  
  
Question Was the US Veterans Affairs initiative to distribute video-enabled tablets during COVID-19   
Question With the emergence of the COVID-19 pandemic, a catastrophic adverse event that has disproportionately impacted Black communities, layered on top of deep-rooted historical inequities (ie, syndemic), how has the postpartum mental health of Black birthing individuals been affected?

Findings In this cohort study of 151 Black participants, perinatal syndemic exposure was associated with negative postpartum mental health outcomes. Specifically, more negative COVID-19 experiences and higher racism scores were associated with increased risk for postpartum depression and anxiety.

Meaning Black birthing individuals already face significant challenges throughout the peripartum period, with adverse associations with mental health, which worsened during the COVID-19 pandemic.  
<https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2790781>

**international perspectives**

**title:** When Hong Kong’s “dynamic zero” covid-19 strategy met omicron, low vaccination rates sent deaths soaring

bmj | 13th april 2022  
  
How did Hong Kong go from being an exemplar of covid-19 control, to the place with the worst covid-19 death rate in the world?

It was a shocking image, unlike anything we had seen before in a Hong Kong hospital,1 even during the devastating SARS outbreak in 2003. A photograph taken on the accident and emergency ward at the Queen Elizabeth Hospital showed three older patients, at least one visibly conscious. Tucked around their beds were six filled body bags on stretchers. The photo circulated on social media on 11 March 2022 and was verified as being taken at the hospital earlier that month. Hong Kong’s mortuaries were full, and clearly no one had a plan to deal with this many dead bodies.

Two weeks before, Hong Kong’s hospitals were already showing signs of being overwhelmed and unprepared for the volume of covid-19 patients—or the resulting deaths. Dozens of mostly older patients were parked in a temporary triage area outside one hospital, some were left up to 24 hours, exposed to the elements in one of the coldest weeks of the year.2 There were other horror stories: infants separated from their parents and admitted to hospital alone3; older patients in a makeshift, government operated isolation facility left for two weeks without bathing4; foreign domestic workers who tested positive for covid-19 turfed out by their employers, sleeping rough, and unable to access government isolation facilities.5

At the end of January 2022, Hong Kong’s confirmed cumulative covid-19 death toll stood at 205 for the entire pandemic.6 Within two months, the toll was 7945 and rising, predominantly among the older population, most of whom were unvaccinated.7

How did Hong Kong go from being an exemplar of covid-19 control, to the place with the worst covid-19 death rate in the world?89 How did things in this highly sophisticated city of 7.4 million people, two years into the pandemic, and a year after the arrival of covid-19 vaccines, go so terribly wrong?...  
<https://www.bmj.com/content/377/bmj.o980>

We

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