COVID-19 weekly update

9th May 2022

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**clinical management**

**title:** Remdesivir and three other drugs for hospitalised patients with COVID-19: final results of the WHO Solidarity randomised trial and updated meta-analyses

the lancet| 2nd may 2022  
  
The Solidarity trial among COVID-19 inpatients has previously reported interim mortality analyses for four repurposed antiviral drugs. Lopinavir, hydroxychloroquine, and interferon (IFN)-β1a were discontinued for futility but randomisation to remdesivir continued. Here, we report the final results of Solidarity and meta-analyses of mortality in all relevant trials to date.

Methods. Solidarity enrolled consenting adults (aged ≥18 years) recently hospitalised with, in the view of their doctor, definite COVID-19 and no contraindication to any of the study drugs, regardless of any other patient characteristics. Participants were randomly allocated, in equal proportions between the locally available options, to receive whichever of the four study drugs (lopinavir, hydroxychloroquine, IFN-β1a, or remdesivir) were locally available at that time or no study drug (controls). All patients also received the local standard of care. No placebos were given. The protocol-specified primary endpoint was in-hospital mortality, subdivided by disease severity. Secondary endpoints were progression to ventilation if not already ventilated, and time-to-discharge from hospital. Final log-rank and Kaplan-Meier analyses are presented for remdesivir, and are appended for all four study drugs. Meta-analyses give weighted averages of the mortality findings in this and all other randomised trials of these drugs among hospital inpatients. Solidarity is registered with ISRCTN, ISRCTN83971151, and ClinicalTrials.gov, NCT04315948.

Findings. Between March 22, 2020, and Jan 29, 2021, 14 304 potentially eligible patients were recruited from 454 hospitals in 35 countries in all six WHO regions. After the exclusion of 83 (0·6%) patients with a refuted COVID-19 diagnosis or encrypted consent not entered into the database, Solidarity enrolled 14 221 patients, including 8275 randomly allocated (1:1) either to remdesivir (ten daily infusions, unless discharged earlier) or to its control (allocated no study drug although remdesivir was locally available). Compliance was high in both groups. Overall, 602 (14·5%) of 4146 patients assigned to remdesivir died versus 643 (15·6%) of 4129 assigned to control (mortality rate ratio [RR] 0·91 [95% CI 0·82–1·02], p=0·12). Of those already ventilated, 151 (42·1%) of 359 assigned to remdesivir died versus 134 (38·6%) of 347 assigned to control (RR 1·13 [0·89–1·42], p=0·32). Of those not ventilated but on oxygen, 14·6% assigned to remdesivir died versus 16·3% assigned to control (RR 0·87 [0·76–0·99], p=0·03). Of 1730 not on oxygen initially, 2·9% assigned to remdesivir died versus 3·8% assigned to control (RR 0·76 [0·46–1·28], p=0·30). Combining all those not ventilated initially, 11·9% assigned to remdesivir died versus 13·5% assigned to control (RR 0·86 [0·76–0·98], p=0·02) and 14·1% versus 15·7% progressed to ventilation (RR 0·88 [0·77–1·00], p=0·04). The non-prespecified composite outcome of death or progression to ventilation occurred in 19·6% assigned to remdesivir versus 22·5% assigned to control (RR 0·84 [0·75–0·93], p=0·001). Allocation to daily remdesivir infusions (vs open-label control) delayed discharge by about 1 day during the 10-day treatment period. A meta-analysis of mortality in all randomised trials of remdesivir versus no remdesivir yielded similar findings.

Interpretation. Remdesivir has no significant effect on patients with COVID-19 who are already being ventilated. Among other hospitalised patients, it has a small effect against death or progression to ventilation (or both).  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00519-0/fulltext>

**title:** When and which patients should receive remdesivir?

the lancet | 2nd may 2022  
  
…These new findings are in line with other publications that show improved outcomes in patients with COVID-19 receiving remdesivir. The common denominator across this research is the reporting of better outcomes during the initial disease stage, when the viral component is high. Physicians should remember that some patients, especially those who are immunocompromised, might have elevated viral loads for months after symptom onset.

Nonetheless, other studies have not shown a positive effect of remdesivir for COVID-19. The most likely explanation for the conflicting findings might be that clinical phenotypes differ among patients. For example, in one of the negative studies, a randomised, double-blind, multicentre trial of remdesivir versus placebo in China, the median time between symptom onset and remdesivir administration was 11 days (IQR 9–12), and 19% of the patients included had undetectable viral RNA on the nasopharyngeal and oropharyngeal swab taken at baseline, despite being PCR-positive at enrolment.

The COVID-19 pandemic has presented various turning points in epidemiology, which are not entirely reflected over the course of the Solidarity trial —for example, the emergence of multiple viral variants causing disease with varying severity and ability for replication, including a SARS-CoV-2 delta variant (B.1.617.2) wave during which young patients often required admission to an intensive care unit quickly after hospitalisation. Due to the inclusion periods established for Solidarity, patients with the delta or omicron (B.1.1.529) variants—which are in current circulation worldwide—were not considered for inclusion in the study. In addition, it is unclear what effect remdesivir or any other antiviral treatment has irrespective of vaccination status. The aim of Solidarity was not to answer this question, of course. Nevertheless, most patients included in Solidarity are unvaccinated, which does not reflect the present reality of the pandemic, where vaccination rates in many countries are high. Knowing the prognostic impact of remdesivir in the current hospitalised population (eg, the older or the immunocompromised), who are likely to be vaccinated, is a needed subject of further research.

Still, the research conducted by the WHO Solidarity Trial Consortium adds meaningfully to the evidence base by demonstrating that we now know remdesivir can reduce the risk of death or progression of mechanical ventilation (or both) in hospitalised patients with COVID-19 requiring oxygen therapy. A great strength of Solidarity is the inclusion of a very large number of patients from many clinical centres around the world. Conversely, the absence of concordance with the current reality—in which patients are likely to be vaccinated and variants continue to emerge—is a limitation. Debate about when and which patients should receive remdesivir or co-adjuvant treatments will, therefore, continue.   
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00789-9/fulltext>

title: COVID-19: REMDESIVIR HAS “SMALL EFFECT” AGAINST DEATH OR PROGRESSION TO VENTILATION, WHO TRIAL FINDS  
  
BMJ| 4th may 2022  
  
With clinical evidence behind it growing, the combination treatment is moving from the laboratory   
effect against death or progression to ventilation among other patients admitted to hospital, the World Health Organization’s Solidarity trial has found. This appears to be a change from findings reported in February 2021, when preliminary trial data suggested that remdesivir “had little or no effect on patients admitted to hospital with covid-19.” The Solidarity trial recruited over 14 000 patients from 454 hospitals across 35 countries between March 2020 and January 2021, of which over 8000 were allocated 1:1 to remdesivir (10 daily infusions) or control (no drug).

The updated results, published in the Lancet, reported that overall 14.5% (602 of 4146) of patients assigned to remdesivir died compared with 15.6% (643 of 4129) assigned to the control group (mortality rate ratio 0.91, 95% confidence interval 0.82 to 1.02, P=0.12). Looking at patients who were already ventilated, 42.1% (151 of 359) assigned to remdesivir died compared with 38.6% (134 of 347) assigned to control (RR 1.13, 95% CI 0.89 to 1.42, P=0.32). For those who were not already ventilated, however, 11.9% in the remdesivir group, compared with 13.5% in the control group, died (RR 0.86, 95% CI 0.76 to 0.98, P=0.02), while 14.1% v 15.7% progressed to ventilation (RR 0.88, 95% CI 0.77 to 1.00, P=0.04). Additionally, when looking at death or progression to ventilation together, the researchers found that the remdesivir group performed better than the control (19.6% v 22.5%, RR 0.84, 95% CI 0.75 to 0.93, P=0.001).

The authors highlighted limitations to their study, including that as high flow and low flow oxygen were not recorded separately at enrolment in the trial, it’s not known whether any protective effect in non-ventilated patients extends to those on high flow oxygen.

Delayed publication. The release of these results has prompted questions about why it has taken so long to publish these data, especially considering WHO’s recommendation against the use of remdesivir in patients with covid-19. Todd Lee, associate professor of medicine, McGill University, and co-investigator on the Canadian arm of Solidarity, told The BMJ, “WHO Solidarity was an important movement towards establishing a global trial during the pandemic. Unfortunately, delays in bringing remdesivir results to co-investigators and the public have likely contributed to under-utilisation of this drug in many jurisdictions. There should be an examination of the reasons for delay and these should inform us that future international endeavours will need to be more agile and transparent.”

Lee and his colleagues published the results from the Canadian arm of the trial in February. They concluded that compared with standard care remdesivir has a “modest but significant effect on outcomes important to patients and health systems, such as the need for mechanical ventilation.” Tom Yates, clinical lecturer at the University College London, has also questioned why the WHO trials team has “sat on these data for more than a year.” “The updated Solidarity results suggest that the drug may offer a meaningful mortality benefit in hospital patients not yet needing mechanical ventilation. WHO should explain why it has taken so long to release these results,” Yates said. “I am surprised that the results were not released as a preprint. Where data may impact practice, as is the case here, it is usual to make the manuscript available while awaiting peer review.”

The BMJ contacted study author and head of the WHO research and development unit Ana-Maria Henao-Restrepo regarding the delay but had not received a response at time of publication.  
<https://www.bmj.com/content/377/bmj.o1118>

**title:** Venovenous extracorporeal membrane oxygenation in patients with acute covid-19 associated respiratory failure: comparative effectiveness study

BMJ| 4th may 2022  
  
Objective To estimate the effect of extracorporeal membrane oxygenation (ECMO) compared with conventional mechanical ventilation on outcomes of patients with covid-19 associated respiratory failure. Design Observational study. Setting 30 countries across five continents, 3 January 2020 to 29 August 2021. Participants 7345 adults admitted to the intensive care unit with clinically suspected or laboratory confirmed SARS-CoV-2 infection. Interventions ECMO in patients with a partial pressure of arterial oxygen to fraction of inspired oxygen (PaO2/FiO2) ratio <80 mm Hg compared with conventional mechanical ventilation without ECMO.

Main outcome measure The primary outcome was hospital mortality within 60 days of admission to the intensive care unit. Adherence adjusted estimates were calculated using marginal structural models with inverse probability weighting, accounting for competing events and for baseline and time varying confounding.

Results 844 of 7345 eligible patients (11.5%) received ECMO at any time point during follow-up. Adherence adjusted mortality was 26.0% (95% confidence interval 24.5% to 27.5%) for a treatment strategy that included ECMO if the PaO2/FiO2 ratio decreased <80 mm Hg compared with 33.2% (31.8% to 34.6%) had patients received conventional treatment without ECMO (risk difference –7.1%, 95% confidence interval –8.2% to –6.1%; risk ratio 0.78, 95% confidence interval 0.75 to 0.82). In secondary analyses, ECMO was most effective in patients aged <65 years and with a PaO2/FiO2 <80 mm Hg or with driving pressures >15 cmH2O during the first 10 days of mechanical ventilation.

Conclusions ECMO was associated with a reduction in mortality in selected adults with covid-19 associated respiratory failure. Age, severity of hypoxaemia, and duration and intensity of mechanical ventilation were found to be modifiers of treatment effectiveness and should be considered when deciding to initiate ECMO in patients with covid-19.  
<https://www.bmj.com/content/377/bmj-2021-068723>

TITLE: Incidence and clinical phenotype of multisystem inflammatory syndrome in children after infection with the SARS-CoV-2 delta variant by vaccination status: a Danish nationwide prospective cohort study  
The Lancet Child & Adolescent Health| 5th may 2022  
  
Background. Multisystem inflammatory syndrome in children (MIS-C) occurs after infection with SARS-CoV-2 and its incidence is likely to depend on multiple factors, including the variant of the preceding SARS-CoV-2 infection and vaccine effectiveness. We aimed to estimate the incidence of MIS-C, and describe the clinical phenotype, following the delta variant of SARS-CoV-2 (B.1.617.2 and sublineages) according to vaccination status. We aimed to compare the incidence and clinical phenotype of MIS-C from our cohort during the pre-delta era.  
  
Methods. This prospective, population-based cohort study included patients aged 0–17 years hospitalised with MIS-C in Denmark, according to the US Centers for Disease Control and Prevention case definition, from Aug 1, 2021, to Feb 1, 2022, a period dominated by the delta variant. We identified MIS-C cases via a nationwide research collaboration involving real-time data collection from all 18 paediatric departments. Aggregated number of SARS-CoV-2 infections by vaccination status was obtained from the Danish COVID-19 surveillance registries. The incidence of MIS-C was calculated using the estimated number of infected individuals by vaccination status. We calculated the incidence of MIS-C per 1 000 000 vaccinated and unvaccinated person-years, and estimated vaccine effectiveness as 1–incidence rate ratio using Poisson regression. Incidence and phenotype of MIS-C were compared with MIS-C cases from the first year of the pandemic. This study is registered at ClinicalTrials.gov, NCT05186597.

Findings. We identified 51 MIS-C cases among unvaccinated individuals and one in a fully vaccinated adolescent. The incidence of MIS-C was one in 3400 unvaccinated individuals (95% CI 2600–4600) with the delta variant and one in 9900 vaccinated individuals (95% CI 1800–390 000) with breakthrough infection. The estimated vaccine effectiveness against MIS-C after the delta variant was 94% (95% CI 55–99; p=0·0061) in individuals aged 5–17 years. The clinical phenotype during the delta wave was comparable to the pre-delta era.

Interpretation. We found the incidence and phenotype of MIS-C in unvaccinated children during the delta wave to be similar to the incidence during the first year of the pandemic. We found vaccine effectiveness to be high against MIS-C, which we suggest was due to protection from infection and, possibly, a decreased incidence of MIS-C after breakthrough infection. Knowledge of the incidence of MIS-C after different SARS-CoV-2 variants and the effect of vaccination might contribute to the elucidation of the extent to which MIS-C is a vaccine-preventable disease.

<https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(22)00100-6/fulltext>

**title:** Acute hepatitis is identified in more children, but cause remains elusive

BMJ | 6th may 2022  
  
UK officials had identified 163 cases of sudden onset hepatitis in children as of 3 May as investigations continued into the cause of the unusually high number of cases.

The UK Health Security Agency (UKHSA) has said that its ongoing investigation continues to suggest an association with adenovirus, as this is the most frequently detected virus in the samples it has tested. Of the 163 children identified with the condition, 11 have received a liver transplant and none have died, said the UKHSA. Jaundice and vomiting were the most common symptoms experienced by the children affected. The agency warned, “Whilst there is some apparent reduction in confirmed cases in the past two weeks overall in the UK, there are continued new case reports in Scotland, the number of cases pending classification in England is substantial, and the likely reporting lags mean that we cannot yet say there is a decrease in new cases.”

But while its investigation continues to suggest an association with adenovirus, the UKHSA said that it was not common to see hepatitis following adenovirus infection in previously well children, so investigations of other factors that may be contributing to the cases were ongoing. Other potential factors include previous SARS-CoV-2 infection, a change in susceptibility possibly due to reduced exposure during the pandemic, and a change in the adenovirus genome itself.

The agency said that the potential link with adenovirus was undergoing a formal epidemiological study, while research studies of the immune system were being undertaken to determine whether changes in susceptibility or the effect of prior infections could be contributing factors.

It added that no evidence suggested any link to covid-19 vaccines. Most cases of acute hepatitis were occurring in children under 5 years old, who were too young to have received the covid vaccine.

Handwashing. The UKHSA advised the public to adhere to normal hygiene measures including thorough handwashing to reduce the spread of many common infections including adenovirus. Meera Chand, the agency’s director of clinical and emerging infections, said, “It’s important that parents know the likelihood of their child developing hepatitis is extremely low. However, we continue to remind everyone to be alert to the signs of hepatitis—particularly jaundice: look for a yellow tinge in the whites of the eyes—and contact your doctor if you are concerned. “Our investigations continue to suggest that there is an association with adenovirus, and our studies are now testing this association rigorously. We are also investigating other contributors, including prior SARS-CoV-2, and are working closely with the NHS and academic partners to understand the mechanism of liver injury in affected children.”  
<https://www.bmj.com/content/377/bmj.o1156.full>

**title:** Association Between the Use of Psychotropic Medications and the Risk of COVID-19 Infection Among Long-term Inpatients With Serious Mental Illness in a New York State–wide Psychiatric Hospital System

jama network open| 6th may 2022  
  
Question Is psychotropic medication use associated with differences in the risk of COVID-19 infection among adults with serious mental illness?

Findings In this cohort study of 1958 inpatients with serious mental illness in a statewide psychiatric hospital system, the use of second-generation antipsychotic medications was associated with a decreased risk of COVID-19 infection; the largest association was observed with the use of paliperidone. Valproic acid use was associated with an increased risk of infection.

Meaning These results suggest that individual psychotropic medications are associated with differential risks of COVID-19 infection among patients with serious mental illness.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791969>

**title:** Antipsychotics and COVID-19 Outcomes—The Potential Role of the Clinical Setting?

jama network open| 6th may 2022  
  
Nemani and colleagues have recently explored the associations between preexisting exposure to psychotropic medications and COVID-19 infection and mortality risks in a retrospective cohort of 1958 psychiatric inpatients with serious mental illness (affective and nonaffective psychosis). Results show that the use of second-generation antipsychotics, as a class, were associated with significantly decreased odds of infection, whereas the use of mood stabilizers was associated with increased odds of infection. When adjusting for sociodemographic and other medical variables, paliperidone use was associated with a decreased risk of infection, and valproic acid use was associated with an increased risk of infection. No significant association with mortality risk emerged in adjusted estimates.

The association of the use of psychopharmacologic compounds, in particular antipsychotics, with severe COVID-19 outcomes is a current matter of debate, with inconsistent findings between studies.2-4 A growing body of literature suggests that the antiviral properties of antipsychotic medications may play a role.5 On the other hand, antipsychotics are known to potentially precipitate cardiovascular and thromboembolic risk and cause drug-drug interactions between antipsychotic medications and COVID-19 medications.6 Nevertheless, for patients with serious mental illness, the lack of psychopharmacologic treatment and poor treatment adherence represent relevant risk factors for psychiatric relapse, reduced global functioning, decreased adherence to health care recommendations, and increased all-cause mortality…   
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791974>

**long-term effects**

**title:** Long COVID: aiming for a consensus  
  
the lancet respiratory medicine| 4th may 2022  
  
Only around one in four people who had covid-19 reported feeling fully recovered within a year of   
The spectrum of signs and symptoms that can newly occur and persist for months to years after SARS-CoV-2 infection was initially named long COVID. This term was collectively created by the patient community in the spring of 2020, and was later followed by other terms, such as post-COVID-19 condition, post-acute sequelae of SARS-CoV-2 infection, and post-COVID syndrome.

This condition can affect different organs and body systems, with a wide range of signs and symptoms reported. Given the magnitude of the sequelae of SARS-CoV-2 infection, it is essential to agree upon the nomenclature and definition to assess its incidence, subtypes, and severity. This process cannot be left to agencies, health-care providers, or researchers alone, but requires extensive consultation, notably including the people affected…  
<https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00135-7/fulltext>

**title:** Caring for the carers: understanding long covid in our diverse healthcare workforce  
  
BMJ| 6th may 2022  
  
Background. The objective of this study was to describe 12-month mortality following SARS-CoV-2   
In the United Kingdom (UK), there have been over 21.4 million confirmed cases of covid-19 as of April 2022.1 Evidence has emerged that some patients are experiencing long term symptoms and complications that extend beyond the acute infection phase, which is now widely known as long covid.23 According to the most recent UK Government’s Office for National Statistics data (April 2021), approximately 1.7 million individuals in the UK reported experiencing covid-19 symptoms for longer than four weeks.4 Of these, 690% had covid-19 for the first time at least 12 weeks previously, and 45% had covid-19 at least a year ago.

As the covid-19 pandemic has progressed, there has been increasing evidence that healthcare workers, especially those from ethnic minority backgrounds, may be at particularly high risk of poor physical and mental health outcomes.5 This is likely to be attributed to the many challenges that healthcare workers face while working in these circumstances, including the high work demand, shortage of staff, lack of personal protective equipment (PPE), rapid changes in protocols and guidance, and long working hours, as well as their increased risk of covid-19 infection and severe disease.56 As a result, healthcare workers may also be more likely than the general population to be affected by long covid, with a disproportionate burden among ethnic minorities.

In response to the potential consequences of long covid, a wide range of nationally funded research studies have been initiated in the UK to better understand the long term impact of SARS-CoV-2 infection on physical and mental health, and how to enhance the diagnosis and treatment of long covid.7 However, these studies have largely, to date, focused on the general population, with a critical gap in research on long covid among healthcare workers, and ethnic minority groups in particular.

Healthcare workers from diverse ethnic backgrounds play a vital role in our response to the covid-19 pandemic, comprising around 42% of doctors and more than 19% of other clinical staff (e.g., nurses, paramedics, midwives), within the NHS workforce.8 The disproportionate impact of covid-19 on healthcare workers has serious implications for the effective operation of the health system. However, up until now, there has been limited attention to how post acute illness and long covid are affecting the home and work lives of healthcare workers, and those from ethnic minority backgrounds in particular. Furthermore, the burden of long covid and its ongoing mental, physical, and occupational impacts on this population are still unknown. This scarcity of literature is particularly problematic for this novel and poorly understood condition, with critical implications for the sustainable delivery of safe and high quality care.

The recent omicron wave has resulted in an increase in covid-19 cases in the UK since early March. Data from the Office for National Statistics (ONS) suggest that in March and early April covid-related deaths in England were at the highest level since mid February. NHS hospitals are once again under pressure as the number of patients admitted to hospital with covid-19 is high. In addition, staff absences from covid-19 are also high. Protecting the occupational health of NHS staff in light of the ongoing pandemic is therefore crucial. Research in this area, looking at the prevalence of long covid among healthcare workers will be vital in generating key recommendations and personalised interventions for addressing social and health inequities. It will also provide critically needed evidence on the physical, mental, and occupational health needs of the diverse NHS workforce, and associated interventional studies, to improve public health as well as the design and delivery of health services for long covid. Research that enables the promotion of progressive and equitable policy interventions in this area will go a long way in helping us achieve this ambition.  
<https://www.bmj.com/content/377/bmj.o1152>

**rates and variants**

**title:** Covid-19: True global death toll from pandemic is almost 15 million, says WHO

BMJ| 6th may 2022

The global number of deaths caused by covid-19 has been severely under-reported, the World Health Organization has said. It estimates that 14.9 million direct and indirect deaths occurred from SARS-CoV-2 in 2020 and 2021—almost three times the 5.4 million reported by governments around the world.

The undercount is the result of a lack of covid-19 testing and death certification, said William Msemburi, technical officer at WHO. Seventy countries do not produce cause of death certificates, he said, and even before the pandemic six in every 10 deaths went unreported…  
<https://www.bmj.com/content/377/bmj.o1144>

**title:** Counting the global COVID-19 dead

BMJ| 6th may 2022

…The global number of deaths caused by covid-19 has been severely under-reported, the World  
Estimates for deaths from the 1918–19 influenza pandemic range widely, from 40 million to 100 million. A century later, a modern effort to count the global COVID-19 dead should be a priority. Mortality data not only meet our moral duty to those who died and their families but are also of enormous practical use to explain the widespread variation in COVID-19 infection that preliminary data have revealed, and its consequences.9  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00845-5/fulltext>

**title:**  Covid-19: US passes one million deaths as mask mandates return  
  
BMJ |6th may 2022  
  
The US passed one million deaths from covid-19 on 4 May 2022, data from NBC News showed.1 This is the world’s highest reported death toll, although deaths are thought to be undercounted. Per capita, Peru has the highest death toll. Reports of US deaths were slightly lower from other sources: Johns Hopkins University reported 996 541, the New York Times 995 715, and the Centers for Disease Control and Prevention (CDC) 994 187. The CDC said that more than 80% of US deaths had been among unvaccinated people. However, during the omicron surge in January and February this year some 42% of deaths were among vaccinated people. Most were over 75s who had been vaccinated but had not received boosters. In the past two weeks cases of covid-19 have increased by 54% and hospital admissions by 19%, but deaths have dropped by 3%.3 The rise in cases is thought to be caused by the omicron subvariants BA.2.12.1 and BA.2.12…  
<https://www.bmj.com/content/377/bmj.o1147>

**title:** Outcomes of SARS-CoV-2 omicron infection in residents of long-term care facilities in England (VIVALDI): a prospective, cohort study

the lancet health longevity| 1st may 2022  
  
Background. The SARS-CoV-2 omicron variant (B.1.1.529) is highly transmissible, but disease severity appears to be reduced compared with previous variants such as alpha and delta. We investigated the risk of severe outcomes following infection in residents of long-term care facilities.

Methods. We did a prospective cohort study in residents of long-term care facilities in England who were tested regularly for SARS-CoV-2 between Sept 1, 2021, and Feb 1, 2022, and who were participants of the VIVALDI study. Residents were eligible for inclusion if they had a positive PCR or lateral flow device test during the study period, which could be linked to a National Health Service (NHS) number, enabling linkage to hospital admissions and mortality datasets. PCR or lateral flow device test results were linked to national hospital admission and mortality records using the NHS-number-based pseudo-identifier. We compared the risk of hospital admission (within 14 days following a positive SARS-CoV-2 test) or death (within 28 days) in residents who had tested positive for SARS-CoV-2 in the period shortly before omicron emerged (delta-dominant) and in the omicron-dominant period, adjusting for age, sex, primary vaccine course, past infection, and booster vaccination. Variants were confirmed by sequencing or spike-gene status in a subset of samples.

Results. 795 233 tests were done in 333 long-term care facilities, of which 159 084 (20·0%) could not be linked to a pseudo-identifier and 138 012 (17·4%) were done in residents. Eight residents had two episodes of infection (>28 days apart) and in these cases the second episode was excluded from the analysis. 2264 residents in 259 long-term care facilities (median age 84·5 years, IQR 77·9–90·0) were diagnosed with SARS-CoV-2, of whom 253 (11·2%) had a previous infection and 1468 (64·8%) had received a booster vaccination. About a third of participants were male. Risk of hospital admissions was markedly lower in the 1864 residents infected in the omicron-period (4·51%, 95% CI 3·65–5·55) than in the 400 residents infected in the pre-omicron period (10·50%, 7·87–13·94), as was risk of death (5·48% [4·52–6·64] vs 10·75% [8·09–14·22]). Adjusted hazard ratios (aHR) also indicated a reduction in hospital admissions (0·64, 95% CI 0·41–1·00; p=0·051) and mortality (aHR 0·68, 0·44–1·04; p=0·076) in the omicron versus the pre-omicron period. Findings were similar in residents with a confirmed variant.

Interpretation. Observed reduced severity of the omicron variant compared with previous variants suggests that the wave of omicron infections is unlikely to lead to a major surge in severe disease in long-term care facility populations with high levels of vaccine coverage or natural immunity. Continued surveillance in this vulnerable population is important to protect residents from infection and monitor the public health effect of emerging variants.  
<https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(22)00093-9/fulltext>

**title:** Omicron infection milder in nursing home residents  
  
The Lancet Healthy Longevity |5th may 2022  
  
…Although these results are positive for nursing home residents, they might only partially alleviate the burdens faced by nursing home staff and administrators. As the dominant SARS-CoV-2 variant changed from delta to omicron, the rate of both hospital admissions (10·5% vs 4·5%) and deaths (12·8% vs 5·3%) among residents decreased. Unfortunately, the relative transmissibility of omicron means that the absolute number of residents affected nearly doubled. During the 103 days included in the delta predominant period, COVID-19 infections led to the hospital admission of 42 residents and deaths of 51 residents. During the much shorter omicron predominant period (51 days), COVID-19 infections led to the hospital admissions of 84 residents and deaths of 99 residents. Unfortunately, these numbers do not yet portend a decrease in the burden of caring for nursing home residents. In addition to continued primary prevention with vaccines, widespread availability of effective antiviral medications and monoclonal antibodies might bring much needed respite for exhausted and overworked nursing home staff and administrators.  
<https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(22)00101-5/fulltext>

**infection control**

**title:** Adequacy of Serial Self-performed SARS-CoV-2 Rapid Antigen Detection Testing for Longitudinal Mass Screening in the Workplace  
  
jama network open |6th may 2022  
  
Question Can untrained persons correctly perform and interpret the results of SARS-CoV-2 rapid antigen detection tests (RADT), and can performance be optimized?

Findings In this cross-sectional study of 278 participants self-performing SARS-CoV-2 RADT in an intended-use setting, the accuracy of RADT interpretation was poor when the manufacturer’s instructions were used. A modified quick reference guide was associated with significantly better user performance.

Meaning These findings suggest that longitudinal mass RADT testing for SARS-CoV-2 could be accurately self-performed in an intended-use setting but there are potential interventions to optimize performance.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791971>

**title:** Sixty seconds on . . . nasal vaccines

BMJ| 6th may 2022  
  
Haven’t my nostrils been through enough? Now, now. You must admit the nasal swab has proved invaluable in the pandemic. And it seems vaccine developers are interested in this orifice too. Trials on 12 potential nasal vaccine candidates against SARS-CoV-2 are currently underway.

What do we nose so far? The covid-19 vaccines we use at the moment are all delivered through an intramuscular injection and have been shown to reduce severe illness and death. Nasal vaccines may be able to go a step further, however, by blocking infections completely at the site of entry. Plus, they would have the added bonus of needle free delivery.

Sinus up! Researchers at Lancaster University have developed one such nasal spray candidate, based on a poultry virus, and are now beginning human trials. During the preclinical phase, they reported that the spray “significantly reduced lung pathology, inflammation, and clinical disease” in rodents. Virologist Muhammad Munir said, “Our studies demonstrate that induction of a local immune response at the point of entry of SARS-CoV-2 has the potential not only to limit clinical disease but also—and perhaps even more importantly—virus transmission from infected to uninfected people.”1

Smells like teen spirit. The lack of needles means nasal sprays are often used in children and teenagers. However, their potential to block infection and even transmission means that, in the case of SARS-CoV-2, there could be benefit in rolling them out to a much wider population.

So what’s the blockage? Nasal vaccines are quite tricky, especially as scientists do not know that much about mucosal immunity. In practice, ensuring that a person gets the right dose and doesn’t just sneeze out or swallow the vaccine can be troublesome, and from there the vaccine still needs to get past the mucus. Researchers also have to consider the closeness of the brain and ensure any vaccine does not cause neurological problems.

That’s a blow. It’s certainly not easy, but that doesn’t mean it’s impossible. Speaking at the Bill Gates book launch event this week, professor of vaccinology at Oxford University, Sarah Gilbert, who led development of the Oxford AstraZeneca covid-19 vaccine, sounded positive. “We have new technology coming through—for example, a spray you take up the nose. I’m hopeful about the advances made with the delivery of these mucosal delivery vaccines,” she said.  
<https://www.bmj.com/content/377/bmj.o1148>

**title:** Studies Examine Risk of Hearing Loss After COVID-19 Vaccination

JAMA network | 3rd may 2022  
  
Objective To evaluate the impact of vaccine scale-up on population level covid-19 mortality and   
Two recent studies investigated the risk of sudden sensorineural hearing loss (SSNHL) after COVID-19 vaccination. In the first study, vaccination was associated with a slightly higher risk of SSNHL in a large Israeli population. But a second study, published in the same issue of JAMA Otolaryngology–Head & Neck Surgery, found no increased SSNHL incidence after vaccination in the US.  
<https://jamanetwork.com/journals/jama/article-abstract/2791709>

**title:** Covid-19: Campaign takes on Pfizer’s “profiteering”  
  
BMJ |3rd MAY 2022  
  
Campaigners from the People’s Vaccine Alliance last week dumped wheelbarrows and sacks full of fake cash outside Pfizer’s UK offices in Surrey to highlight what they claim is the company’s pandemic profiteering. The protest was part of a campaign mounted by 20 global health organisations that sent an open letter to the company warning its executives they had “blood on their hands” because of its monopolies on covid-19 vaccine and treatment technologies. The letter stated that, though Pfizer almost doubled its annual revenue to $81.3bn (£65bn; €77.3bn) in 2021, it has contributed to a 15 billion dose gap in global supplies needed for 2022.

The World Health Organizationb has also named Pfizer among the drug companies which it believes should be doing more to improve covid vaccine equity and access…  
<https://www.bmj.com/content/377/bmj.o1111>

**title:** No minister, a “protective ring” was not thrown around care homes

BMJ| 3rd may 2022  
  
Margaret Thatcher famously said “Advisers advise, ministers decide.”1 Yet, throughout the covid-19 pandemic this distinction has often seemed blurred. Ministers justified decisions by claiming they were “following the science.” But were they? Numerous accounts suggest not.234 Their defence is that the situation was extremely challenging. There were still many uncertainties about the nature of the new infection and how it was transmitted. Their opportunities to respond were constrained, for example, by limited testing capacity and an already overstretched health system. So, were ministerial decisions reasonable in the circumstances? In at least one area, the discharge of patients from hospitals into care homes, contributing to thousands of avoidable deaths, we can now say with certainty that they were not…  
<https://www.bmj.com/content/377/bmj.o1116>

**title:** DOES THE WORLD STILL NEED NEW COVID-19 VACCINES?

new england journal of medicine| 4th may 2022

Although there was a global shortage of Covid-19 vaccines in 2021, by mid 2022, the vaccine supply will no longer be a limiting factor in efforts to provide more equitable coverage. As of April 19, 2022, approximately 11.5 billion Covid-19 vaccine doses have been administered globally.1 Scaling up manufacturing capacity for currently available vaccines at the speed promised by vaccine producers through the COVAX (Covid-19 Vaccines Global Access) program and beyond should secure the coverage target projected by the World Health Organization (WHO) for 70% of the world population by mid 2022.2 So why do we still need new Covid-19 vaccines?

A total of 344 Covid-19 vaccine candidates have been developed or are still in development.3 Of these, 31 vaccine products are already in large-scale use after conditional approval by national regulatory authorities or under the WHO Emergency Use Listing. At least five different technology platforms have been used (i.e., messenger RNA [mRNA], viral-vectored, inactivated whole-virus, protein subunit, and plasmid DNA approaches). Several of the inactivated whole-virus and protein subunit vaccines need adjuvants to potentiate the immune response.

Many reasons dictate a need for the development of a range of Covid-19 vaccines available for use across the world with the aim of bringing the pandemic under control. Each vaccine product has different attributes and advantages and disadvantages, and multiple factors must be considered to guide policy decisions. Different countries and health care settings, as well as different subpopulations and age groups, may benefit from different vaccine products developed on different platforms. Efficacy and safety, as evaluated in phase 3 trials, are not the sole outcomes to be assessed in a country’s decision to procure and introduce new Covid-19 vaccines. Ease of schedules, vaccine effectiveness when used in routine programs, need and frequency of boosters, cost, considerations regarding cold-chain logistics, manufacturing scalability, acceptability by communities, and scope for local or regional production are additional important factors…  
<https://www.nejm.org/doi/full/10.1056/NEJMe2204695>

**title:** Efficacy and Safety of the RBD-Dimer–Based Covid-19 Vaccine ZF2001 in Adults

NEW ENGLAND JOURNAL OF MEDICINE| 4TH MAY 2022  
  
The ZF2001 vaccine, which contains a dimeric form of the receptor-binding domain of severe acute respiratory syndrome coronavirus 2 and aluminum hydroxide as an adjuvant, was shown to be safe, with an acceptable side-effect profile, and immunogenic in adults in phase 1 and 2 clinical trials.

Methods. We conducted a randomized, double-blind, placebo-controlled, phase 3 trial to investigate the efficacy and confirm the safety of ZF2001. The trial was performed at 31 clinical centers across Uzbekistan, Indonesia, Pakistan, and Ecuador; an additional center in China was included in the safety analysis only…  
<https://www.nejm.org/doi/full/10.1056/NEJMoa2202261>

**title:** Efficacy and Safety of a Recombinant Plant-Based Adjuvanted Covid-19 Vaccine

NEW ENGLAND JOURNAL OF MEDICINE| 4TH MAY 2022  
  
Coronavirus-like particles (CoVLP) that are produced in plants and display the prefusion spike glycoprotein of the original strain of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are combined with an adjuvant (Adjuvant System 03 [AS03]) to form the candidate vaccine.

Methods. In this phase 3, multinational, randomized, placebo-controlled trial conducted at 85 centers, we assigned adults (≥18 years of age) in a 1:1 ratio to receive two intramuscular injections of the CoVLP+AS03 vaccine or placebo 21 days apart. The primary objective of the trial was to determine the efficacy of the CoVLP+AS03 vaccine in preventing symptomatic coronavirus disease 2019 (Covid-19) beginning at least 7 days after the second injection, with the analysis performed after the detection of at least 160 cases…  
<https://www.nejm.org/doi/full/10.1056/NEJMoa2201300>

**title:** Effectiveness of Ad26.COV2.S and BNT162b2 Vaccines against Omicron Variant in South Africa [coreespondence]  
  
bmj | 29th april 2022  
  
Government policy that exposed thousands of vulnerable elderly people in England to SARS-CoV-2 in   
The B.1.1.529 (omicron) strain of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly become dominant among the variants of concern in the coronavirus disease 2019 (Covid-19) pandemic in all regions of the world. The omicron variant now accounts for 95.4% of genetic sequences of SARS-CoV-2 in Africa, 96.0% in North America, and 87.6% in South America. This variant has been shown to escape antibody neutralization by both the BNT162b2 messenger RNA vaccine (Pfizer–BioNTech) and the Ad26.COV2.S vaccine (Johnson & Johnson–Janssen),1,2 which are the only two Covid-19 vaccines that have been administered in South Africa. We established the early effectiveness of the two-dose BNT162b2 vaccine regimen during the omicron-driven fourth wave in South Africa.2 The national vaccine program in South Africa has distributed 26,262,060 doses of the BNT162b2 vaccine and 8,477,267 doses of the Ad26.COV2.S vaccine. As of May 1, 44.8% of adults in South Africa had been fully vaccinated with two doses of the BNT162b2 vaccine or a single dose of the Ad26.COV2.S vaccine. Assessing vaccine effectiveness is critical for national vaccine programs…  
<https://www.nejm.org/doi/full/10.1056/NEJMc2202061>

**title** Immunogenicity and safety of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine in people living with and without HIV-1 infection: a randomised, controlled, phase 2A/2B trial  
  
the lancet HIV | may 2022  
  
There is a paucity of data on COVID-19 vaccines in people living with HIV-1, who could be at increased risk of severe illness and death from COVID-19. We evaluated the safety and immunogenicity of a Matrix-M adjuvanted recombinant spike protein nanoparticle COVID-19 vaccine (NVX-CoV2373; Novavax) in HIV-negative people and people living with HIV-1.

Methods. In this randomised, observer-blinded, multicentre, placebo-controlled phase 2A/B trial in South Africa, participants aged 18–84 years, with and without underlying HIV-1, were enrolled from 16 sites and randomly assigned (1:1) to receive two intramuscular injections of NVX-CoV2373 or placebo, 21 days apart. People living with HIV-1 were on stable antiretroviral therapy and had an HIV-1 viral load of less than 1000 copies per mL. Vaccine dosage was 5 μg SARS-CoV-2 recombinant spike protein with 50 μg Matrix-M adjuvant, whereas 0·9% saline was used as placebo injection (volume 0·5 mL each). All study staff and participants remained masked to study group assignment. We previously reported an interim analysis on the efficacy and safety of the NVX-CoV2373 vaccine (coprimary endpoints). In this Article, we present an expanded safety analysis for the full cohort of participants and report on the secondary objective of vaccine immunogenicity in the full cohort of people living with HIV-1 and in HIV-negative individuals overall and stratified by baseline SARS-CoV-2 serostatus. This trial is registered with ClinicalTrials.gov, NCT04533399, and the Pan-African Clinical Trials Registry, PACTR202009726132275.

Findings. Participants were enrolled between Aug 17 and Nov 25, 2020. The safety analysis set included 4164 HIV-negative participants (2089 in the intervention group and 2075 in the placebo group) and 244 people living with HIV-1 (122 in the intervention group and 122 in the placebo group). 1422 (34·1%) of 4164 HIV-negative people and 83 (34·0%) of 244 people living with HIV-1 were categorised as baseline SARS-CoV-2-positive (ie, anti-spike IgG reactive at enrolment or had a reactive SARS-CoV-2 nucleic acid amplification test by 14 days after the second study vaccination). In the NVX-CoV2373 group, solicited local and systemic adverse events were more common in HIV-negative participants (427 [30·6%] local and 401 [28·7%] systemic) than in people living with HIV-1 (20 [25·3%] local and 20 [25·3%] systemic) among those who were baseline SARS-CoV-2-seronegative (naive). Of the serious adverse events that occurred among HIV-negative people (of whom, two [0·1%] were baseline SARS-CoV-2-negative and four [0·6%] were baseline SARS-CoV-2-positive) and people living with HIV-1 (for whom there were no serious adverse events) in the NVX-CoV2373 group, none were assessed as related to the vaccine. Among participants who were baseline SARS-CoV-2-negative in the NVX-CoV2373 group, the anti-spike IgG geometric mean titres (GMTs) and seroconversion rates (SCRs) were lower in people living with HIV-1 (n=62) than in HIV-negative people (n=1234) following the first vaccination (GMT: 508·6 vs 1195·3 ELISA units [EU]/mL; SCR: 51·6% vs 81·3%); and similarly so 14 days after the second vaccination for GMTs (14 420·5 vs 31 631·8 EU/mL), whereas the SCR was similar at this point (100·0% vs 99·3%). In the NVX-CoV2373 group, anti-spike IgG GMTs 14 days after the second vaccination were substantially higher in those who were baseline SARS-CoV-2-positive than in those who were baseline SARS-CoV-2-seronegative for HIV-negative participants (100 666·1 vs 31 631·8 EU/mL) and for people living with HIV-1 (98 399·5 vs 14 420·5 EU/mL). This was also the case for angiotensin-converting enzyme 2 receptor-binding antibody and neutralising antibody titres.

Interpretation. The safety of the NVX-CoV2373 vaccine in people living with HIV-1 was similar to that in HIV-negative participants. However, people living with HIV-1 not previously exposed to SARS-CoV-2 had attenuated humoral immune responses to NVX-CoV2373 compared with their HIV-negative vaccine counterparts, but not so if they were baseline SARS-CoV-2-positive.  
<https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00041-8/fulltext>

**title:** HIV and COVID-19: juxtaposition of two pandemics  
  
THE LANCET HIV | MAY 2022  
  
The emergence of SARS-CoV-2 in 2019 has led to a juxtaposition of two pandemics: COVID-19 and HIV/AIDS. As of March 27, 2022, the world has reported more than 480 million confirmed cases of COVID-19 and more than 6 million deaths. HIV/AIDS continues to be a major global public health pandemic: more than 37 million people were living with HIV at the end of 2020, two-thirds of whom (an estimated 25 million) are in sub-Saharan Africa.

At the individual level, the COVID-19 pandemic has important implications for people living with HIV and has affected the delivery of HIV services. In this issue of The Lancet HIV, two remarkable studies assess the effectiveness of COVID-19 vaccination in HIV-positive individuals. In one study, Lucas Netto and colleagues studied people living with HIV at the University of Sao Paulo, Brazil.

They compared CoronaVac immunogenicity responses in people living with HIV with CD4 counts less than 500 cells per μL with people living with HIV with CD4 counts of 500 cells per μL or more. Immunogenicity was reduced in those with CD4 counts less than 500 cells per μL, suggesting that these individuals could be at increased risk of an inadequate antibody response to vaccines. However, these results do not corroborate other findings from recent studies that found similar immunogenicity following other types of COVID-19 vaccines (eg, ChAdOx1 and BNT162b2) in people living with HIV compared to controls.

In a second study, Shabir Madhi and colleagues studied NVX-CoV2373 vaccine immunogenicity in people with HIV compared with HIV-negative individuals and stratified by baseline SARS-CoV-2 serostatus. The safety of NVX-CoV2373 in people living with HIV was similar to that in those who were HIV-negative. However, people with HIV who were not previously exposed to SARS-CoV-2 had attenuated humoral immune responses to NVX-CoV2373 compared with their HIV-negative vaccine counterparts. It is unknown if the difference in the immunological responses observed in the study by Netto and colleagues and those by others using the ChAd0x1 and BNT162b2 vaccines were due to the type of the vaccines used. At any rate, both studies clearly suggest the need for strategies to improve vaccine immunogenicity in people living with HIV. The peculiarity in people living with HIV is the compromised immune system from chronic HIV infection and the use of antiretroviral therapy, which might increase the risk of SARS-CoV-2 infection and mortality from COVID-19. People with HIV with low CD4 counts and those not on antiretroviral therapy might have the greatest risk of developing severe symptoms of COVID-19 or not controlling SARS-CoV-2.

Vaccination of people living with HIV is essential as these individuals might not clear SARS-CoV-2 virus effectively, which could lead to the emergence of new variants. In addition, unvaccinated people with HIV are four times more likely than HIV-negative people to experience symptoms of long COVID after acute COVID-19 illness. These symptoms are associated with higher levels of inflammatory markers. Two-thirds of people living with HIV are in Africa. However, only 15% of the 1·3 billion people living on the continent have been fully vaccinated. Vaccine inequity in low-income and middle-income countries (LMICs), especially where the burden of HIV/AIDS is high, will obviously lead to limited access to vaccines for people living with HIV. Because vaccines are steadily becoming available in LMICs, coordinated efforts and partnerships are needed to scale up vaccination and delivery in these countries. This is the only way that people living with HIV will be able to access COVID-19 vaccination.

The juxtaposition of the COVID-19 and HIV pandemics also has a tremendous impact on HIV service delivery. In South Africa, for instance, because of the COVID-19 pandemic and responses to it, there was a substantial decline in the number of people living with HIV starting treatment and an estimated 47% decrease in HIV testing in April, 2020. Disruptions to HIV services could lead to worse outcomes for those with HIV and potentially increased HIV transmission. As such, addressing co-morbidities and ensuring a secure supply of antiretroviral therapy for people living with HIV during the COVID-19 pandemic is crucial. Delivery platforms for HIV services have been used to scale up COVID-19 vaccination in some African countries, such as Lesotho. Such platforms could facilitate access to vaccination for people living with HIV. Longitudinal studies are also needed to gain further insights into responses to different COVID-19 vaccines in people living with HIV.  
<https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00095-9/fulltext>

**title:** Why covid vaccine studies are still needed  
  
BMJ | 5th may 2022  
  
We still have much to learn from research on covid-19 vaccines, says Andrew Ustianowski

With spring booster jabs being deployed across the UK for people aged 75 and over and those with suppressed immune systems, many may assume that research on covid-19 vaccines is now complete. However, as we all know, SARS-CoV-2 has the ability to mutate, leading to new waves of covid-19 infection that can cause illness and death, strain healthcare services, and harm the economy. This is why vaccine research remains vital to our ongoing protection from covid-19. The National Institute for Health and Care Research (NIHR) continues to lead and support studies on booster vaccines, because we believe it can give us a better understanding about how vaccines work against different variants and for different people. Continued research into which combinations of vaccines (both existing and new) work best in different populations (the general population, immunosuppressed people, pregnant women, those in low and middle income countries, etc) is vital to help us all stay protected.

In the UK, the Joint Committee on Vaccination and Immunisation (JCVI) will continue to provide the government and public with the latest vaccination advice, shaped by study findings and real time data. To achieve the most accurate and effective vaccine guidance, researchers need to continuously update departments like the JCVI with detailed data. As researchers continue to investigate SARS-CoV-2 and the vaccines we’ve created, the results of these studies may point to the need for a continuous approach to research. We may need to provide regular boosters to sections of our population for the next few years and ongoing research will be required to ensure we give the most effective vaccines at appropriate intervals.

Alternatively, we may gather enough intelligence to enable us to look at creating something that can pre-empt future variants. A vaccine that is capable of tackling all types of coronavirus—including MERS or even the common cold—would be the utopia. We therefore need several different types of studies to enhance scientific understanding in a number of areas and to inform how we proceed.

Firstly, we need to fully understand how different vaccine regimens best protect us. To see what works well now, what will work best throughout 2022, and what will work better in the longer term, covid-19 vaccine studies are continuing to launch, recruit participants, and publish findings. Several booster studies continue to enrol individuals, and collect and crunch the data that have been collected since last year. Studies such as COV-BOOST continue to show us the most effective booster combinations of several vaccines currently available and in development, to guide our short term booster programmes. Whereas the Octave-DUO study is determining how to best protect those with compromised immune systems.

Secondly, as more vaccines are approved for use, our approach can become more granular and precise. Although the majority of the UK population has been vaccinated, there are still particular population subgroups who would benefit from specific further research. The current guidance from JCVI has helped inform policy for these groups; however, to better understand the immune response of younger people, pregnant women, older people, and those with comorbidities and suppressed immune systems, further booster studies are vital.

Finally, covid-19 vaccine research is now analysing the effectiveness of both adapted booster jabs to target specific variants and vaccines that could target multiple and future variants. The currently recruiting Moderna Omicron vaccine study (and the Pfizer study in the US) is looking to understand the former by investigating if its tweaked RNA vaccines can better target and prevent infection from the latest covid-19 variant. Meanwhile, Gritstone, one of the world’s first multi-variant covid-19 vaccine studies, which I am the chief investigator on, is an example of the latter. This study is in the early stages of research and hopes to boost the immune response of participants to a wide array of variants. This approach, if successful, could remove the inevitable lag time that arises when you’re “tail chasing” a vaccine adapted for a specific, newly identified variant.

Many people might assume that because boosters are being administered, the job of vaccine researchers is done. Or, that because we’re once again rolling out a booster programme for those over 75 and people who are more vulnerable, it means we’re resigned to being stuck in a loop of regular, perhaps yearly, vaccines. However, this may not necessarily be the case, and ongoing research could change how and when vaccines are delivered.

Further vaccine research can help us stay ahead of this pandemic, ease the stress on healthcare staff and infrastructure delivering jabs, and allow us to be better prepared for any future pandemics. So much progress within immunisation technology and knowledge has been made in the past two years that the possibility of a universal covid-19 vaccine isn’t out of the question, and what we’ve learnt may be successfully applied to wider research, including vaccines for influenza, HIV, and other infections. We may even end up with a vaccine that tackles all types of coronavirus, including the common cold—something that was blue sky thinking just a few years ago.  
<https://www.bmj.com/content/377/bmj.o1135>

**title:** Closing the global vaccine equity gap: equitably distributed manufacturing  
  
NEW ENGLAND JOURNAL OF MEDICINE| 28TH april 2022  
  
…The world cannot afford a protracted pandemic with ongoing damage to economic productivity and global health security. A collaborative public–private effort to direct and inform an equitably distributed vaccinated manufacturing capacity is a decisive step towards pandemic resilience. The World Economic Forum in collaboration with the US National Academy of Medicine and the Coalition for Epidemic Preparedness Innovations is spearheading such an effort: the Collaborative on Equitable Vaccine Manufacturing Capacity, which will be launched later in May, 2022. All stakeholders must act now to work collectively and collaboratively. Only through an aligned and systematic approach will it be possible to end the present COVID-19 pandemic, stave off future pandemics, and finally realise the shared vision of global vaccine equity.  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00793-0/fulltext>

**HEALTH MANGEMENT & workforce well-being**

**title:** Stop doctors from retiring to boost elective recovery workforce, says NHS England

BMJ | 6th may 2022  
  
Employing retired doctors and attempting to persuade those planning their retirement to begin a new career chapter in the NHS instead are among a list of measures devised by NHS England to help hospitals tackle the covid-19 backlog.

The 11 “high impact enablers” (see box) were sent to all English trusts in a letter on 3 May, aiming to shore up the workforce to optimise elective capacity. Crucially, however, the advice omits any measures that would remove the tax burdens that disincentivise many experienced doctors, particularly consultants, from working for the NHS beyond pensionable age. In response, the BMA called the omission “extremely disappointing.” Vishal Sharma, BMA consultants committee chair, said, “The recognition that doctors who are either approaching retirement age or have recently retired should be supported to remain in the workforce by allowing them to work differently and more flexibly is welcome and long overdue. “However, this letter fails to mitigate the punitive pension taxation that we know is driving experienced and much needed doctors away in their droves.”

Sharma said the BMA has contacted NHS England several times to ask that it takes meaningful steps to fix the problem and correct misleading information on its website about NHS pensions.2 “In an example on the NHS England website, rather than receiving a higher pension by staying for an extra year and continuing to contribute towards their pension, a consultant would instead be tens of thousands of pounds worse off over the course of their retirement,” he said.

The BMA would like the tax disincentive removed. It has asked for the NHS scheme to become a tax unregistered pension scheme, similar to the one the government introduced for the judiciary. Under such a scheme, employees do not receive tax relief on employee pension contributions and, as such, their pension savings are not tested against the annual or lifetime allowance measures that limit or claw back tax relief, meaning the tax burden would substantially reduce. Beyond the pension matter, Sharma said that the pandemic had laid bare the fact that the NHS does not have enough doctors. “What’s worse is that the doctors we have are exhausted, burnt out, and demoralised. They gave their all during the pandemic and are now facing the secondary challenge of tackling enormous waiting lists,” he said. “The government must commit to appropriately increasing the size of the workforce. The forthcoming government commissioned workforce strategy must lay out a clear plan to achieve this.”

The letter from five directors at NHS England asks trust leaders to continue the “local innovation and grassroots improvement activity” that benefited patients during the pandemic. It encourages creative solutions to job roles and ways of working. “As a national team we will be supportive of organisations who are innovative in this area. We will work with you to provide support. We seek to remove barriers to support the aims of the changes you are planning.”

In response, the Royal College of Surgeons of England broadly welcomed the ideas. However, college president Neil Mortensen, warned, “The biggest challenge remains the availability of staff. There are 110 000 vacancies in the NHS and this is adding pressure to an already overstretched workforce. We need to make sure there are enough staff now and in the future to care for our patients. This means both support for surgical trainees and a credible long term workforce plan from government.” Chief executive of NHS Providers, Chris Hopson, said that trust leaders were already implementing a range of initiatives to reduce waiting times for treatments but there was no disguising the fact that the “NHS simply doesn’t have enough staff.” “Asking existing staff to do more isn’t enough,” he said. “We need a long term, fully funded workforce plan.”

Recommended measures to boost workforce

-1 Removing caps on consultant job plans so they can exceed 10 programmed activities a week

-2 Support educational, training, and leadership time for consultants

-3 Encourage recently retired staff to return to work

-4 Encourage staff considering retirement to stay

-5 Create options for all staff to increase their contracted hours, including through bank shifts to reduce reliance on locum and agency staff

-6 Maximise the use of collaborative staff banks

-7 Attract paid staff and volunteers who have helped to deliver local vaccination programmes to take up NHS roles

-8 Increase capacity during peak periods of leave by effective rostering and planning leave within teams

-9 Use NHS reservists to support surges and peaks in activity

-10 Use alternative staffing models to support increased care delivery within safe staffing parameters—including students, trainees, and support workers

-11 Accelerate recruitment of substantive posts—nurses, midwives, administrative staff, healthcare support workers, and medical support workers  
<https://www.bmj.com/content/377/bmj.o1145>

**title:** Rammya Mathew: Tough times ahead for a depleted workforce

BMJ | 5th may 2022  
  
The recent changes to covid-19 restrictions indicate a new phase of the pandemic, where we are supposedly learning to live with the virus. Masks are not required, testing is no longer readily available to the public, and isolation has become optional rather than mandatory.

I’m sure that many businesses are pleased to see an end to testing and isolation, in the hope that covid-19 related absences among their workforce will now rapidly decline. But what about the NHS? Last month the remaining population controls against covid-19 ended. As a result, cases of covid-19 rose steeply throughout the population, leading to high absences rates among NHS staff as they were off sick or needed to self-isolate.12 This has inevitably meant cancelling operations, outpatient appointments, and diagnostic tests. We’re still declaring covid outbreaks on many of our wards—leading to fewer available hospital beds, which has a further detrimental impact on waiting lists and patient flow through the NHS.

When the message being relayed to the public is that the pandemic is virtually over and that the NHS is in some sort of accelerated recovery mode, it’s no wonder that patients have a low tolerance for more news of cancellations. It’s adding fuel to the fire, when public satisfaction with the NHS is already at its lowest recorded level since 1997.3

Last week NHS England announced that infection and prevention control measures introduced during the pandemic were being relaxed, partly to help free up capacity in healthcare services to tackle the huge treatment backlog. I’m afraid that, no matter what infection prevention and control measures we take in the workplace, we’ll inevitably still be exposed to the virus in our lives outside work. This is crippling our ability to do the much needed catch-up work now facing almost every sector of the health service.

Worn-out NHS workers are the ones caught in the middle of this bind—either through being acutely unwell with covid and having to take time off or through being left to work in understaffed departments, unable to provide a decent service. I dread to think of the impact of long covid on top of this, as it’s yet to be fully felt or at least captured in available statistics—but recent data from the Office for National Statistics warn that many of the people affected will probably have symptoms for a year or even longer. Suffice it to say, this is not the recovery that any of us had anticipated or hoped for. With a stretched, depleted, and unwell workforce, the NHS’s staff and its patients have tough times ahead.  
<https://www.bmj.com/content/377/bmj.o1090>

**title:** The Health Service And Social Care Workers (Scrutiny Of Coronavirus-Related Deaths) (Revocation) Directions 2022

DEPARTMENT OF HEALTH & SOCIAL CARE | 3rd may 2022  
  
These directions revoke The Health Service and Social Care Workers (Scrutiny of Coronavirus-related Deaths) Directions 2020 which ensured that NHS trusts and NHS foundation trusts sought and prioritised the services of medical examiners to scrutinise the deaths of health service and adult social care staff with coronavirus.  
<https://kingsfund.blogs.com/health_management/2022/05/the-health-service-and-social-care-workers-scrutiny-of-coronavirus-related-deaths-revocation-directi.html>

**recovery**

**title:** COVID-19: the next phase and beyond

the lancet | 7th may 2022  
  
After living for more than 2 years with COVID-19—with over 6·2 million confirmed deaths (but probably many more, with an estimated 20 million excess deaths) and over 510 million confirmed cases—the world is at a critical point. The omicron wave, with its high transmissibility and milder course than previous variants, especially for people who are fully vaccinated and without comorbidities, is abating in many countries. Restrictions are being relaxed, and people are slowly returning to pre-pandemic activities, including gatherings, office-based working, and cultural events. Mask mandates are being lifted in many countries. Testing and surveillance have decreased and travelling is recommencing widely. People are understandably exhausted and want to forget about the pandemic. This would be a grave mistake…  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00817-0/fulltext>

**title:** Harnessing COVID-19 Data Through Collaboration—The Consortium of HCA Healthcare and Academia for Research Generation  
  
jama health forum | 6th may 2022  
  
What should a health system do when in possession of the largest and most coherent data set that could help accelerate the understanding of COVID-19 and its treatment? For HCA Healthcare, a large health care organization comprised of 185 hospitals and more than 2000 sites of care in 20 US states and the UK, the answer to this question was a matter of social responsibility: harness the potential of this asset through data sharing and research collaborations with public-sector and academic institutions. Although straightforward in concept, this goal was technically and ethically complex. By building on a legacy of multi-institution research partnerships and in conjunction with the Agency for Healthcare Research and Quality (AHRQ), a COVID-19 research consortium known as CHARGE (Consortium of HCA Healthcare and Academia for Research Generation) was rapidly initiated…  
<https://jamanetwork.com/journals/jama-health-forum/fullarticle/2791961>

**title:** Can the world become a place where the planet and all people flourish after the pandemic?

BMJ | 3rd May 2022  
  
Covid-19 has impeded achievement of the sustainable development goals and a radical rethink of the global economy is required to meet them argue Fran Baum and colleagues

In 2015, the world adopted 17 sustainable development goals (SDGs) with 169 targets to be achieved by 2030. These goals aimed to create a world in which people and the planet flourish. They were more ambitious than the previous millennium development goals and linked human wellbeing with the sustainability of the planet. Achieving these goals would make the world fairer, more sustainable, biodiverse, and healthy as well more participatory, decolonised, and democratic. Yet even before the covid-19 pandemic concerns emerged about whether governments had the will to achieve these aspirational goals. Covid-19 has cast further doubt and seen reversals rather than progress on many of the goals.

We examine the effect of covid-19 on progress across the five inter-related dimensions of the SDGs—planet, people, prosperity, peace, and partnership1—and discuss the political, social, and economic transformations required to meet them…  
<https://www.bmj.com/content/377/bmj-2021-067872>

**title:** Choices that fail health and wellbeing [editorial]

bmj | 5th may 2022  
  
Would you spend £2bn of taxpayers’ money on an unproved treatment for covid-19 (doi:10.1136/bmj.o1053)?1 Would you spend that money in the throes of a cost of living crisis that is worsening the health of people on low incomes and forcing people with cancer to turn off their heating (doi:10.1136/bmj.o938, doi:10.1136/bmj.o1103)?23 Wouldn’t you wait for better evidence to emerge (doi:10.1136/bmj.o1037)?

Would you continue to deny staff respiratory protection in defiance of the evidence and the airborne nature of SARS-CoV-2 transmission (doi:10.1136/bmj.o1082)?5 Would you continue to maintain that you had no idea that asymptomatic transmission of the virus was possible in defiance of the fact that you, your science advisers, and the available evidence had acknowledged this possibility from the outset (doi:10.1136/bmj.o1116)?6 Would you show no remorse over a High Court verdict that condemns you for failing vulnerable patients by discharging them to social care from hospital beds without a covid test (doi:10.1136/bmj.o1098)? …  
<https://www.bmj.com/content/377/bmj.o1115>

**title:** The end of great expectations?

BMJ | 5th may 2022  
  
The pandemic inquiry must account for stalling life expectancy before the pandemic

Life expectancy at birth is a key summary measure of the health of any given population. Ideally, it should increase steadily over time in the absence of data artefact, mass migration in or out, or a large scale event such as war or natural disaster, disease outbreak, or societal collapse. Any break in the trend beyond isolated annual fluctuations should raise the alarm among health workers, policy makers, and the public. The covid-19 pandemic has caused life expectancy to fall below predicted levels worldwide, including in the UK.1 Part of this may have been inevitable given what we now know about this new coronavirus, but part could have been avoided. The inquiry into the UK government’s handling of the pandemic is essential, not least to provide answers to the tens of thousands of bereaved families who are rightly asking whether more could have been done to save their loved ones.

When the UK inquiry takes place—public hearings are likely to begin in 2023 (the Scottish government’s inquiry may start in 2022)3—it must also consider what was happening in the UK before the pandemic began. This is essential to ensure that the population harms caused by covid-19 are measured accurately, taking full account of prevailing trends before the pandemic…  
<https://www.bmj.com/content/377/bmj-2022-071329>

**title:** The Potential Legacy Of The Pandemic On Mortality

Covid-19 Actuaries Response Group | 9th may 2022  
  
The impact of Covid-19 on mortality can be broadly split into three categories: direct impacts; indirect impacts; and wider social and economic impacts. Indirect impacts represent excess deaths due to stresses on the health system or changes in the health-seeking behaviour of individuals. These are the focus of this bulletin. At this stage of the pandemic, the mortality impacts are shifting from direct to indirect. Analysing emerging data can help to identify the magnitude of these impacts and the extent to which they are asymmetric across the population. If care pathways do not rapidly return to pre-pandemic levels, then the Covid-19 pandemic will affect the standard of healthcare, morbidity and mortality across the UK for years to come.  
<https://kingsfund.blogs.com/health_management/2022/05/the-potential-legacy-of-the-pandemic-on-mortality.html>

**public health & health inequalities**

**title:** COVID-19 pandemic: what's next for public health?

the lancet public health | may 2022  
  
Two years after SARS-COV-2 was declared a public health emergency, global estimates of excess deaths from the Institute for Health Metrics and Evaluation indicate that 18·2 million people died due to the pandemic by Dec 31, 2021—three times higher than official records suggest. 100 million people have been plunged into extreme poverty by the pandemic, according to World Bank estimates. While the true burden of COVID-19 is being unravelled, is a mental health crisis being unmasked? The pandemic has exposed long-standing gaps and a global underinvestment in mental health care and prevention, disproportionately affecting young people and women. According to WHO's Mental Health Atlas, the global median spending on mental health is still hovering at around 2% of government health expenditure. However, cases of anxiety disorders rose by 25·6% and cases of major depressive disorder increased by 27·6% globally in 2020. Immediate action is needed to strengthen mental health services to address this steeply increasing demand and to meet peoples’ needs...  
<https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(22)00095-0/fulltext>

We

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

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

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