COVID-19 weekly update

6th June 2022

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**clinical management**

**title:** Final results of the DisCoVeRy trial of remdesivir for patients admitted to hospital with COVID-19 [correspondence]

the lancet infectious diseases| june 2022  
  
We reported the preliminary results of the DisCoVeRy trial regarding the efficacy and safety of remdesivir in hospitalised patients with COVID-19 in February, 2022. Remdesivir did not have a clinical or virological benefit in the studied population. Notably, the number of patients included was lower than initially expected, because inclusions in this trial group were prematurely stopped by the data and safety monitoring board. Here, after completion of data monitoring, we report the final analysis, including two secondary endpoints that were not previously reported. Full results regarding secondary outcomes are available elsewhere.

Two secondary endpoints were not previously reported: in-hospital mortality and mortality at 3 months after randomisation. Remdesivir did not have a significant effect on in-hospital mortality (33 of 420 participants in the remdesivir group vs 38 of 423 participants in the control group; adjusted OR 0·84 [95% CI 0·51–1·37]; p=0·48), nor on mortality at 3 months (43 of 420 vs 49 of 423; 0·87 [0·56–1·36]; p=0·55). Similar to findings from preliminary analyses, participants from the remdesivir group who were not on mechanical ventilation or ECMO when they were randomly assigned to a treatment group (n=692) had a significantly longer time to the composite endpoint of new mechanical ventilation, ECMO, or death in the 29 days following randomisation than did the control group (cumulative incidence in the remdesivir group was 58 [17%] of 343 participants vs 88 [25%] of 349 in the control group; adjusted hazard ratio [HR] 0·63 [95% CI 0·45–0·88]; p=0·010). In non-prespecified analyses, this effect was significant in participants with severe disease when they were randomly assigned to a treatment group (cumulative incidence in the remdesivir group 25 [29%] of 87 vs 47 [50%] of 94 in the control group; unadjusted HR 0·49 [95% CI 0·30–0·80]; p=0·0040) but not in those with moderate disease (33 (13%) of 256 vs 41 (16%) of 255; 0·79 [0·50–1·25]; p=0·31). No significant effect of remdesivir on the viral kinetics was observed (effect of remdesivir on the slope of decrease of the nasopharyngeal viral load was –0·006 log10 copies per 10 000 cells per day [95% CI –0·02 to 0·03]; p=0·66).

Among the 833 participants included in the safety analysis (remdesivir, n=410; control, n=423), no significant difference was evidenced in the occurrence of grade 3–4 adverse events (143 of 410 participants in the remdesivir group vs 150 of 423 participants in the control group; unadjusted OR 0·98 [95% CI 0·73–1·32]; p=0·91) nor of serious adverse events (147 of 410 vs 138 of 423; 1·17 [0·87–1·57]; p=0·29).

Overall, the final results of the DisCoVeRy trial for the efficacy and safety of remdesivir reinforce the observations in the preliminary report, supporting recommendations against its use in hospitalised patients with COVID-19.  
<https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00295-X/fulltext>

**title:** The future of Paxlovid for COVID-19

jama | 17th may 2022  
  
…The US Government pays around US$530 for each 5-day course of Paxlovid. The drug is a combination of ritonavir plus the novel protease inhibitor PF-07321332. The emergency use authorisation was granted late last year, on the strength of results from the phase 2–3 trial showing that Paxlovid reduces the risk of hospitalisation or death for high-risk patients by 88%, compared with the placebo, if given within 5 days of symptom onset. The trial only recruited unvaccinated individuals. But three-quarters of the UK population and two-thirds of the US population are now fully vaccinated against COVID-19.

“It is clear that antivirals have an important role early in the course of illness for people whose immune systems are not working well, or who have not responded well to the vaccine”, said Charlotte Summers, professor of intensive care medicine at the University of Cambridge (Cambridge, UK). “We still do not have evidence on whether Paxlovid prevents hospitalisation or severe illness in people who have been vaccinated.” The UK-based PANORAMIC trial is examining the use of antivirals in patients who have not been hospitalised, regardless of vaccination status. On April 12, Paxlovid was added to the trial…  
<https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00192-8/fulltext>

**title:** Baricitinib versus dexamethasone for adults hospitalised with COVID-19 (ACTT-4): a randomised, double-blind, double placebo-controlled trial

the lancet respiratory medicine| 23rd may 2022  
  
…In hospitalised patients with COVID-19 requiring supplemental oxygen by low-flow, high-flow, or non-invasive ventilation, baricitinib plus remdesivir and dexamethasone plus remdesivir resulted in similar mechanical ventilation-free survival by day 29, but dexamethasone was associated with significantly more adverse events, treatment-related adverse events, and severe or life-threatening adverse events. A more individually tailored choice of immunomodulation now appears possible, where side-effect profile, ease of administration, cost, and patient comorbidities can all be considered….  
<https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00088-1/fulltext>

**title:** Outcomes of the SARS-CoV-2 omicron (B.1.1.529) variant outbreak among vaccinated and unvaccinated patients with cancer in Europe: results from the retrospective, multicentre, OnCovid registry study  
  
THE LANCET ONCOLOGY | 2ND JUNE 2022

Background. The omicron (B.1.1.529) variant of SARS-CoV-2 is highly transmissible and escapes vaccine-induced immunity. We aimed to describe outcomes due to COVID-19 during the omicron outbreak compared with the prevaccination period and alpha (B.1.1.7) and delta (B.1.617.2) waves in patients with cancer in Europe…  
  
Interpretation. Despite time-dependent improvements in outcomes reported in the omicron phase compared with the earlier phases of the pandemic, patients with cancer remain highly susceptible to SARS-CoV-2 if they are not vaccinated against SARS-CoV-2. Our findings support universal vaccination of patients with cancer as a protective measure against morbidity and mortality from COVID-19.  
<https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(22)00273-X/fulltext>

**title:** Prognostic implications of comorbidity patterns in critically ill COVID-19 patients: A multicenter, observational study

the lancet regional health europe| 27th may 2022  
  
Background. The clinical heterogeneity of COVID-19 suggests the existence of different phenotypes with prognostic implications. We aimed to analyze comorbidity patterns in critically ill COVID-19 patients and assess their impact on in-hospital outcomes, response to treatment and sequelae.

Methods. Multicenter prospective/retrospective observational study in intensive care units of 55 Spanish hospitals. 5866 PCR-confirmed COVID-19 patients had comorbidities recorded at hospital admission; clinical and biological parameters, in-hospital procedures and complications throughout the stay; and, clinical complications, persistent symptoms and sequelae at 3 and 6 months.

Findings. Latent class analysis identified 3 phenotypes using training and test subcohorts: low-morbidity (n=3385; 58%), younger and with few comorbidities; high-morbidity (n=2074; 35%), with high comorbid burden; and renal-morbidity (n=407; 7%), with chronic kidney disease (CKD), high comorbidity burden and the worst oxygenation profile. Renal-morbidity and high-morbidity had more in-hospital complications and higher mortality risk than low-morbidity (adjusted HR (95% CI): 1.57 (1.34-1.84) and 1.16 (1.05-1.28), respectively). Corticosteroids, but not tocilizumab, were associated with lower mortality risk (HR (95% CI) 0.76 (0.63-0.93)), especially in renal-morbidity and high-morbidity. Renal-morbidity and high-morbidity showed the worst lung function throughout the follow-up, with renal-morbidity having the highest risk of infectious complications (6%), emergency visits (29%) or hospital readmissions (14%) at 6 months (p<0.01).

Interpretation. Comorbidity-based phenotypes were identified and associated with different expression of in-hospital complications, mortality, treatment response, and sequelae, with CKD playing a major role. This could help clinicians in day-to-day decision making including the management of post-discharge COVID-19 sequelae.  
<https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00116-8/fulltext>

**title:** Genetic and Clinical Characteristics of Patients in the Middle East With Multisystem Inflammatory Syndrome in Children

jama network open| 31st may 2022  
  
Question What are the clinical, genetic, and laboratory characteristics of Middle Eastern patients with multisystem inflammatory syndrome in children (MIS-C)?

Findings In this cohort study of 45 patients with MIS-C of primarily Arab and Asian origins, an enrichment of rare, likely deleterious immune-related genetic variants was found, with a possible association between genetic findings and MIS-C onset and resistance to treatment.

Meaning These findings suggest that comprehensive genetic profiling of patients with MIS-C of diverse ethnicities is essential to characterize the genetic contribution to this disease.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2792814>

**title:** Sotrovimab drives SARS-CoV-2 omicron variant evolution in immunocompromised patients [correspondence]

the lancet microbe| 27th may 2022  
  
…As previously reported for patients treated with bamlanivimab, we urge to consider monoclonal antibody as monotherapy in immunocompromised patients as a risk for escape mutant selection that might hamper viral clearance. Immunocompromised patients treated with monoclonal antibodies should benefit from a reinforced virological follow-up, including viral sequencing and viral load assessment.  
<https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(22)00120-3/fulltext>

**title:** Severe hospital events following symptomatic infection with Sars-CoV-2 Omicron and Delta variants in France, December 2021–January 2022: A retrospective, population-based, matched cohort study

the lancet eclinical medicine| 1st june 2022  
  
Background. A rapid increase in incidence of the SARS-CoV-2 Omicron variant (sub-lineage BA.1) occurred in France in December 2021, while the Delta variant was prevailing since July 2021. We aimed to determine whether the risk of a severe hospital event following symptomatic SARS-CoV-2 infection differs for Omicron versus Delta.

Methods. We conducted a retrospective cohort study to compare severe hospital events (admission to intensive care unit or death) between Omicron and Delta symptomatic cases matched according to week of virological diagnosis and age. The analysis was adjusted for age, sex, vaccination status, presence of comorbidities and region of residence, using Cox proportional hazards model.

Findings. Between 06/12/2021–28/01/2022, 184 364 cases were included, of which 931 had a severe hospital event (822 Delta, 109 Omicron). The risk of severe event was lower among Omicron versus Delta cases; the difference in severity between the two variants decreased with age (adjusted Hazard Ratio (aHR)=0·13 95%CI: 0·08–0·20 among 40–64 years, aHR=0·50 95%CI: 0·26–0.98 among 80+ years). The risk of severe event increased with the presence of comorbidities (for very-high-risk comorbidity, aHR=4·15 95%CI: 2·86–6·01 among 40–64 years) and in males (aHR=2·28 95%CI: 1·82–2·85among 40–64 years) and was higher in unvaccinated compared to primo-vaccinated (aHR=7·29 95%CI: 5·58–9·54 among 40–64 years). A booster dose reduced the risk of severe hospital event in 80+ years infected with Omicron (aHR=0·29; 95%CI: 0·12–0·69).

Interpretation. This study confirms the lower severity of Omicron compared to Delta. However, the difference in disease severity is less marked in the elderly. Further studies are needed to better understand the interactions between age and severity of variants.  
<https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(22)00185-7/fulltext>

**long-term effects**

**title:** Covid-19: Two million people in the UK are estimated to be experiencing long covid, says ONS

BMJ| 1st june 2022  
  
Around two million people in the UK are estimated to be experiencing long covid symptoms, the Office for National Statistics has said. The figure, based on self-reported symptoms and not a clinical diagnosis, comes from an analysis of 296 868 responses to the Coronavirus (Covid-19) Infection Survey, collected over the four week period ending 1 May 2022. Participants were asked if they are still experiencing symptoms, that are not explained by something else, more than four weeks after first having covid-19. The estimates are based on a representative sample of people living in private households and do not include those in communal establishments such as halls of residence, prisons, schools, hospitals, or care homes.

Long covid symptoms adversely affected the day-to-day activities of 1.4 million people (71%) of those who self-reported long covid, with 20% reporting that their ability to go about day-to-day activities had been “limited a lot.” Fatigue was the most common symptom reported (55% of those who self-reported long covid), followed by shortness of breath (32%), a cough (23%), and muscle ache (23%).

Of the two million, 1.4 million had covid-19 at least 12 weeks previously, while 826 000 had it at least one year previously and 376 000 said they had it at least two years previously. Self-reported long covid was highest in people aged 35 to 69; women; people living in more deprived areas; those working in social care, education, or healthcare; and those with another health condition or disability. Of people with self-reported long covid, 30% first had covid-19 before alpha became the dominant variant, compared with 12% in the alpha period, 21% in the delta period, and 31% in the omicron period…  
<https://www.bmj.com/content/377/bmj.o1391>

**title:** Long term implications of covid-19 in pregnancy  
  
BMJ| 31st may 2022  
  
Complications in pregnancy, including maternal and perinatal deaths, increased with each wave of the covid-19 pandemic. By contrast, serious illness fell in other high risk groups because of vaccines and approved treatments.1 More than a year after the UK’s Joint Committee on Vaccination and Immunisation (JVCI) opened up covid-19 vaccination to pregnant women, 40% of women giving birth have still not received a first dose.2 This is despite a positive benefit-risk profile, endorsement in guidelines, and public health campaigns. Worryingly, 69.5% of black women giving birth have not received any covid-19 vaccine.2

Meanwhile the JCVI has chosen not to include pregnant women in its interim autumn booster plans.3 Strategies for treating covid-19 in pregnancy and potential long term complications are also underused.1 A large portion of the diffidence for both vaccination and treatment in pregnancy stems from the continued exclusion of pregnant women from much of the pre-approval drug development process. This results in delayed or even absent data on benefit-risk profiles and a dangerous spiral of indecision.

The public health implications for postpartum women are unclear, but some key considerations are increased cardiovascular risk, including in future pregnancies; the impact of long covid; and the effect of ethnic and socioeconomic inequalities that widened during the pandemic.4 The downstream amplification of cardiovascular risk for women who have covid-19 in pregnancy must not be overlooked. Covid-19 during pregnancy substantially increases the risk of pre-eclampsia,5 which could increase cardiovascular disease later in life.6 In addition, acute covid-19 significantly increases the risks and one year burden of cardiovascular disease in the general population.7

The UK is ideally placed to define these risks more precisely, taking a life course approach and using NHS data in either anonymised or consented cohorts. Observational studies to understand covid-19’s long term effect in babies have begun, but a deeper understanding of the biological mechanisms at play and effects on whole populations are needed….  
<https://www.bmj.com/content/377/bmj-2022-071296>

**title:** What People Have Told Us About Long Covid: September 2020 – March 2022  
  
healthwatch england| 1st june 2022  
  
Healthwatch looked at a sample of 122 people’s experiences, shared with them between September 2020 and March 2022, to explore what it is like for people seeking help with symptoms of long Covid. Key findings set out in this briefing include: GPs are unsure of the symptoms of long Covid; GPs are unaware of what support is on offer or how to access it; and long Covid can affect every aspect of life, but patients are not being offered holistic support.  
<https://kingsfund.blogs.com/health_management/2022/06/what-people-have-told-us-about-long-covid-september-2020-march-2022-.html>

**title:** Helen Salisbury: Living under the long shadow of covid

BMJ| 24th may 2022  
  
The number of patients with acute covid-19 is falling, says the weekly survey from the Office for National Statistics (ONS), although cases in England are still 20 times higher than this time last year.1 A few months ago I was receiving a dozen notifications of new infections each day; this has now slowed to a trickle, although some of this is attributable to the lack of a mechanism for patients to report the results of self-bought tests. This restriction gives the impression that the UK Health Security Agency doesn’t actually want information about infections, which seems at odds with its remit to protect public health.

While we cross our fingers and hope that the next wave isn’t already on its way (and with decreased surveillance, we may not get much warning), “long covid” consultations have overtaken acute ones. I don’t know how many patients on my list have prolonged symptoms after covid infection: I speak to some regularly and have referred them to the local long covid clinic, but there will be more I don’t know about, who have simply reduced their activity and are battling on, assuming that nothing much can be done. I’m also seeing patients with non-specific symptoms such as fatigue, headache, and “brain fog” who ask me, “Is this because I had covid?” The only honest answer is that I don’t know, but there seems to be a lot of it about…  
<https://www.bmj.com/content/377/bmj.o1288>

**infection control**

title: COVID-19 vaccine effectiveness against the omicron (BA.2) variant in England  
  
the lancet infectious diseases|24th may 2022  
  
In this Comment, we estimate vaccine effectiveness against symptomatic disease and hospitalisation with BA.1 and BA.2 after one or two doses of BNT162b2, ChAdOx1-S, or mRNA-1273, and after booster doses of BNT162b2 or mRNA-1273 during a period of co-circulation…  
<https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00309-7/fulltext#:~:text=25%20weeks%20or%20more%20after,72%C2%B72)%20against%20BA>

**title:** Effectiveness of mRNA vaccine boosters against infection with the SARS-CoV-2 omicron (B.1.1.529) variant in Spain: a nationwide cohort study

the lancet infectious diseases| 2nd june 2022  
  
The omicron (B.1.1.529) variant of SARS-CoV-2 has increased capacity to elude immunity and cause breakthrough infections. The aim of this study was to estimate the effectiveness of mRNA-based vaccine boosters (third dose) against infection with the omicron variant by age, sex, time since complete vaccination, type of primary vaccine, and type of booster…  
[Full text](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00292-4/fulltext#:~:text=In%20this%20nationwide%20representative%20study,to%2034%20days%20after%20administration.)  
[Commentary](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900319-X/fulltext)

**title:** Longitudinal variation in SARS-CoV-2 antibody levels and emergence of viral variants: a serological analysis

the lancet microbe| 27th may 2022  
  
Serological assays are being used to monitor antibody responses in individuals who had SARS-CoV-2 infection and those who received a COVID-19 vaccine. We aimed to determine whether such assays can predict neutralising antibody titres as antibody levels wane and viral variants emerge…  
<https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(22)00090-8/fulltext>

**title:** Association of COVID-19 Vaccination During Pregnancy With Incidence of SARS-CoV-2 Infection in Infants  
  
jama internal medicine|1st june 2022  
  
Question Is maternal COVID-19 vaccination during the second or third trimester of pregnancy associated with reduced risk of COVID-19 within the first 4 months of life in their infants?

Findings In this register-based cohort study of all live-born infants in Norway, there was a lower incidence of a positive SARS-CoV-2 test result in infants born to women vaccinated with a messenger RNA vaccine during pregnancy. The risk was lower during the period dominated by the Delta variant than during the Omicron-dominated period.

Meaning The study results suggest that maternal COVID-19 vaccination during pregnancy could protect against infant SARS-CoV-2 infection in the early months of life.  
<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2793109>

**title:** COVID-19 mRNA vaccine in pregnancy: Results of the Swiss COVI-PREG registry, an observational prospective cohort study

the lancet regional health europe| 29th may 2022  
  
Short term benefits are seen after a second covid-19 vaccine booster—normally a fourth vaccine   
Pregnant individuals with coronavirus disease 2019 (COVID-19) are at increased risk of severe disease, prematurity, and stillbirth. In March 2021, vaccination for at risk pregnant women was recommended in Switzerland, expanding this to all pregnant women in May 2021. Our aim was to assess the safety of mRNA COVID-19 vaccines in pregnancy…  
  
…Frequent local and systemic effects were described after exposure to mRNA COVID-19 vaccines during pregnancy but severe events were rare. Women vaccinated during pregnancy did not experience higher adverse pregnancy or neonatal outcomes when compared to historical data on background risks in the obstetric population.  
[Full text](https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00104-1/fulltext#:~:text=We%20found%20that%20pregnant%20women,in%20pregnant%20women%20seemed%20safe.)

**title:** BALANCING RISK AND BENEFIT OF SARS-COV-2 VACCINES IN CHILDREN

the lancet regional health europe| 29th may 2022

…This rigorous study confirms a link between SARS-CoV-2 mRNA vaccines and occurrence of MIS-C and myocarditis in children aged 12-17. However, rates of both of these complications are low compared with the rate of MIS-C after natural infection. As the mRNA vaccines appear to be effective in preventing MIS-C as well as severe COVID 5,6 this study provides reassuring data that will be of help to policy makers, parents and paediatricians. Despite vaccines being associated with rare inflammatory complications, the risk benefit ratio for SARS-CoV-2 vaccination continues to favour vaccination, at least in the 12-17 year old age group included in this study. The finding of a link between vaccination and MIS-C may also provide a clue to the biological mechanisms underlying MIS-C, as it suggests a prominent role for the spike protein, as the sole viral protein expressed by the mRNA vaccines.

Ouldali and colleagues should be congratulated for conducting such a large scale, rigorous and important study which has provided clear evidence on which to base policy.

However SARS-CoV-2 is a moving target, and the balance between vaccine induced and infection induced MIS-C and myocarditis, and the efficacy of vaccines, may be different for Omicron and other new variant waves that seem likely to arise. Furthermore, the duration of protection against both MIS-C and severe COVID-19 following vaccination is unknown. Continued surveillance and monitoring of both SARS-CoV-2 infection rates and severity, and complications of vaccines will be needed to guide decisions on how to use the available vaccines in children.  
<https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00106-5/fulltext>

**title:** Evaluation of mRNA-1273 Covid-19 Vaccine in Children 6 to 11 Years of Age

new england journal of medicine| 26th MAY 2022  
  
Vaccination of children to prevent coronavirus disease 2019 (Covid-19) is an urgent public health need. The safety, immunogenicity, and efficacy of the mRNA-1273 vaccine in children 6 to 11 years of age are unknown.

… Two 50-μg doses of the mRNA-1273 vaccine were found to be safe and effective in inducing immune responses and preventing Covid-19 in children 6 to 11 years of age; these responses were noninferior to those in young adults.  
<https://www.nejm.org/doi/full/10.1056/NEJMoa2203315>

**title:** Effectiveness of heterologous and homologous covid-19 vaccine regimens: living systematic review with network meta-analysis

BMJ| 31st MAY 2022  
  
Objective: To evaluate the effectiveness of heterologous and homologous covid-19 vaccine regimens with and without boosting in preventing covid-19 related infection, hospital admission, and death…  
  
…An mRNA booster is recommended to supplement any primary vaccine course. Heterologous and homologous three dose regimens work comparably well in preventing covid-19 infections, even against different variants. The effectiveness of three dose vaccine regimens against covid-19 related death remains uncertain.  
<https://www.bmj.com/content/377/bmj-2022-069989>

**title:** Protection and Waning of Natural and Hybrid Immunity to SARS-CoV-2  
  
new engand journal of medicine | 25th May2022  
  
…Among persons who had been previously infected with SARS-CoV-2 (regardless of whether they had received any dose of vaccine or whether they had received one dose before or after infection), protection against reinfection decreased as the time increased since the last immunity-conferring event; however, this protection was higher than that conferred after the same time had elapsed since receipt of a second dose of vaccine among previously uninfected persons. A single dose of vaccine after infection reinforced protection against reinfection.  
<https://www.nejm.org/doi/full/10.1056/NEJMoa2118946>

**title:** Short term, relative effectiveness of four doses versus three doses of BNT162b2 vaccine in people aged 60 years and older in Israel: retrospective, test negative, case-control study  
  
BMJ | 24th may 2022  
  
Active immunization with the BNT162b2 vaccine (Pfizer–BioNTech) has been a critical mitigation tool   
Objective To examine the relative effectiveness of a fourth dose of the Pfizer-BioNTech mRNA (BNT162b2) vaccine compared with three vaccine doses over the span of 10 weeks.  
  
…Conclusions A fourth dose of the BNT162b2 vaccine appears to have provided additional protection against both SARS-CoV-2 infection and severe covid-19 disease relative to three vaccine doses. However, relative effectiveness of the fourth dose against infection appears to wane sooner than that of the third dose.  
<https://www.bmj.com/content/377/bmj-2022-071113#:~:text=Conclusions%20A%20fourth%20dose%20of,that%20of%20the%20third%20dose>.

**title:** How are vaccines being adapted to meet the changing face of SARS-CoV-2?  
  
BMJ | 1st june 2022  
  
The vaccines’ development was a miracle of modern science—but as SARS-CoV-2 adapts, how are manufacturers and researchers responding? Chris Stokel-Walker learns more

It seems like a lifetime ago, but the first clinically approved vaccine against SARS-CoV-2 was given to a patient just 17 months ago, on 8 December 2020. Since that first vaccine dose, developed by the drug company Pfizer, a number of vaccines have been developed. Ten are approved by the World Health Organization, and scores more are still undergoing trials.

However, just as vaccine development hasn’t stood still, neither has the virus itself. The changing face of the novel coronavirus has challenged scientists to modify existing vaccines to better tackle the changing characteristics of SARS-CoV-2. Yet, despite much talk of modified vaccines for variants, the world is still using largely the same original vaccines for initial rollouts and booster doses…  
<https://www.bmj.com/content/377/bmj.o1257>

**title:** Challenges of Deciding Whether and How to Update COVID-19 Vaccines to Protect Against Variants  
  
JAMA | 1st june 2022  
  
Seasonal influenza vaccines are updated every year, depending on what strains are circulating globally, leaving many people—especially those who still contracted COVID-19 after 2 booster shots—wondering why vaccines against SARS-CoV-2 haven’t changed as variants have come and gone. Currently available COVID-19 vaccines are based on the spike protein of Wuhan-Hu-1, the prototype SARS-CoV-2 virus. But the virus has changed significantly since Wuhan-Hu-1 was sequenced in January 2020, with variants of concern ranging from Alpha to Omicron.

Omicron, and especially its subvariants, is so different from Wuhan-Hu-1 that it is most adept at evading the immune response generated by current vaccines. Even so, studies have shown that the prototype COVID-19 vaccines still reduce the risk of serious illness and death from Omicron.

Updating COVID-19 vaccines is easier said than done, and some observers question whether it’s the best way to tackle the unpredictable, ever-changing virus…  
<https://jamanetwork.com/journals/jama/fullarticle/2793149>

**title:** Safety and immunogenicity of a live-attenuated influenza virus vector-based intranasal SARS-CoV-2 vaccine in adults: randomised, double-blind, placebo-controlled, phase 1 and 2 trials  
  
the lancet respiratory medicine | 26th may 2022  
  
All currently available SARS-CoV-2 vaccines are administered by intramuscular injection. We aimed to evaluate the safety and immunogenicity of a live-attenuated influenza virus vector-based SARS-CoV-2 vaccine (dNS1-RBD) administered by intranasal spray in healthy adults…  
  
…dNS1-RBD was well tolerated in adults. Weak T-cell immunity in peripheral blood, as well as weak humoral and mucosal immune responses against SARS-CoV-2, were detected in vaccine recipients. Further studies are warranted to verify the safety and efficacy of intranasal vaccines as a potential supplement to current intramuscular SARS-CoV-2 vaccine pools. Steps should be taken in future studies to reduce the potential for cross-contamination caused by the vaccine strain aerosol during administration.  
<https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00131-X/fulltext>

**title:** Safety and immunogenicity of the SARS-CoV-2 ARCoV mRNA vaccine  
  
the lancet microbe | 31st may 2022  
  
…The safety and immunogenicity of the SARS-COV-2 ARCoV mRNA vaccine has also attracted attention. But the vaccine results are hardly encouraging.1 In terms of safety, the proportion of adverse events, such as fever after one dose of vaccine, was quite high compared with the two main mRNA vaccines on the market,2 which might have something to do with the direct use of unmodified RNA molecules to trigger a strong immune response…  
<https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(22)00150-1/fulltext>

**title:** Assessment of Delayed Large Local Reactions After the First Dose of the SARS-CoV-2 mRNA-1273 Vaccine in Japan  
  
JAMA dermatology | 1st june 2022  
  
Question Are sex and age associated with susceptibility of delayed large local reactions (DLLRs) after the first injection of the SARS-CoV-2 mRNA-1273 vaccine?

Findings In this cross-sectional study of 5893 participants, the incidence rate of DLLRs after the first dose of the mRNA-1273 vaccine was significantly higher among females than among males and among participants aged 30 to 69 years than among adults aged 18 to 29 years.

Meaning The findings suggest that DLLR may be a type IV allergic skin reaction  
<https://jamanetwork.com/journals/jamadermatology/fullarticle/2792873>

**title:** COVID-19 vaccine booster dose needed to achieve Omicron-specific neutralisation in nursing home residents  
  
the lancet ebio medicine | 20th may 2022  
  
Nursing home (NH) residents have borne a disproportionate share of SARS-CoV-2 morbidity and mortality. Vaccines have limited hospitalisation and death from earlier variants in this vulnerable population. With the rise of Omicron and future variants, it is vital to sustain and broaden vaccine-induced protection. We examined the effect of boosting with BNT162b2 mRNA vaccine on humoral immunity and Omicron-specific neutralising activity among NH residents and healthcare workers (HCWs)…  
<https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00247-X/fulltext>

**title:** FIND documents dramatic reduction in COVID-19 testing  
  
the lancet infectious diseases | 2nd june 2022  
  
COVID-19 testing rates, which peaked at the end of 2021, have plummeted worldwide. Bill Rodriguez, head of FIND, warns that countries are “losing visibility”. Ann Danaiya Usher reports…  
<https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00376-0/fulltext?rss=yes>

**title:** Association Between COVID-19 Booster Vaccination and Omicron Infection in a Highly Vaccinated Cohort of Players and Staff in the National Basketball Association  
  
JAMA | 2nd june 2022  
  
…This study found that in a young, healthy, highly vaccinated cohort frequently monitored for SARS-CoV-2, booster vaccination was associated with a significant reduction in incident infections during the Omicron wave. Study limitations include generalizability to older populations and the possibility that some infections may have been undetected in the absence of daily surveillance testing. This is a population that was recently boosted (median of 20 days as of December 1, 2021) and may not reflect waning efficacy over time. Surveillance testing in this population captured both symptomatic and asymptomatic infections, which differs from studies of the effectiveness of boosters that did not assess risk of asymptomatic infections.2,3 Continued research is required to assess the need for additional booster doses beyond a single booster dose.  
<https://jamanetwork.com/journals/jama/fullarticle/2793169>

**title:** Vaccine effectiveness against COVID-19 breakthrough infections in patients with cancer (UKCCEP): a population-based test-negative case-control study  
  
the lancet oncology | 23rd may 2022  
  
People with cancer are at increased risk of hospitalisation and death following infection with SARS-CoV-2. Therefore, we aimed to conduct one of the first evaluations of vaccine effectiveness against breakthrough SARS-CoV-2 infections in patients with cancer at a population level.  
  
In this population-based test-negative case-control study of the UK Coronavirus Cancer Evaluation Project (UKCCEP), we extracted data from the UKCCEP registry on all SARS-CoV-2 PCR test results (from the Second Generation Surveillance System), vaccination records (from the National Immunisation Management Service), patient demographics, and cancer records from England, UK, from Dec 8, 2020, to Oct 15, 2021…  
  
…COVID-19 vaccination is effective for individuals with cancer, conferring varying levels of protection against breakthrough infections. However, vaccine effectiveness is lower in patients with cancer than in the general population. COVID-19 vaccination for patients with cancer should be used in conjunction with non-pharmacological strategies and community-based antiviral treatment programmes to reduce the risk that COVID-19 poses to patients with cancer.  
<https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(22)00202-9/fulltext>

BMJ Commentary: <https://www.bmj.com/content/377/bmj.o1305#:~:text=Vaccination%20was%20found%20to%20offer,months%20after%20the%20second%20dose>.

**HEALTH MANGEMENT & workforce well-being**

**title:** Covid-19: Doctors’ wellbeing must be “critical priority” after pandemic mistakes, says BMA

BMJ| 23rd may 2022  
  
The BMA’s review into the UK’s management of the pandemic found that the government failed in its duty of care to protect doctors and other healthcare staff from avoidable harm. Matthew Limb examines its findings.

On 19 May the BMA published the first two reports of its five part review into the lessons learnt from the covid-19 pandemic, which will inform its submission to the upcoming public inquiry.123

The reports lay bare doctors’ often traumatic experience, with stark personal testimonies and data collected through real time surveys revealing an “exhausted” profession that was let down, left underprotected, and in need of more support to meet unrelenting service pressures.

Ministers must make doctors’ wellbeing a “critical priority” while learning lessons from the “devastating” harms and policy mistakes, the BMA said…  
<https://www.bmj.com/content/377/bmj.o1284>

**title:** David Oliver: No quick staffing fixes for the elective care backlog

BMJ | 1st june 2022  
  
The covid pandemic has had a massive impact on elective care. The National Audit Office has estimated that 12 million patients may be on waiting lists by 2025.

More than 100 000 clinical vacancies are unfilled in the NHS, and the UK already has fewer doctors and nurses per 1000 people than nearly every European or developed country. Only 52% of advertised consultant physician posts across a range of specialties were filled in 2021,1 and an increasing number of doctors and nurses are considering early retirement or leaving the service.23 Many are tired, demoralised, or unwell after two years of providing pandemic medicine.4

The government recently rejected calls for an amendment to the Health and Social Care Act 2022 to mandate regular, transparent workforce planning and reporting, as well as calls for a broader post-covid health and social care recovery plan.56 In this context, on 5 May NHS England published Enabling the Workforce for Elective Recovery,7 proposing some immediate actions…  
<https://www.bmj.com/content/377/bmj.o1337>

**title:** Facilitating Equitable, High-Quality Cancer Screening in the Post–COVID-19 Era [COMMENTARY]

JAMA NETWORK OPEN | 3RD JUNE 2022  
  
By use of self-reported data from the nationally representative Behavioral Risk Factor Surveillance System, Fedewa and colleagues1 document the decrease in cervical and breast cancer screening during 2020, likely secondary to the direct and indirect effects of the COVID-19 pandemic. Decreases in past-year prevalence were greater for segments of the population who, because of structural inequities, were already at higher risk of not undergoing cancer screening before the pandemic and who also were the most likely to experience the adverse consequences of the pandemic (eg, those with lower educational attainment and those who identify as Hispanic).2 These findings raise concerns that the combined effects of the COVID-19 pandemic, both the direct risks associated with COVID-19 incidence and mortality and the indirect risks associated with deferred care for other conditions, could lead to increased all-cause mortality and worsening of health disparities.

Although these findings are alarming, 2 other aspects of the findings from Fedewa and colleagues1 suggest possible routes for addressing current and future inequities…  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2792964?widget=personalizedcontent&previousarticle=2763851>

**title:** The effect of COVID-19 on routine diabetes care and mortality in people with diabetes

the lancet diabetes & endocrinology |27th may 2022  
  
The COVID-19 pandemic has had a disproportionate effect on the health of people living with diabetes. SARS CoV-2 affects many aspects of metabolism, creating the potential for biological interplay and bidirectional negative influence.1 Data from many countries have consistently shown that people with diabetes with COVID-19 have an excess risk of hospital admission, increased disease severity, and increased mortality.2, 3, 4

New data, reported by Jonathan Valabhji and colleagues in The Lancet Diabetes & Endocrinology,5 provides evidence that people with diabetes were affected by the pandemic in more ways than one. Their results show that pandemic-related reductions in care have increased non-COVID-related mortality among people with diabetes.  
<https://www.thelancet.com/journals/landia/article/PIIS2213-8587(22)00162-0/fulltext#:~:text=Data%20from%20many%20countries%20have,disease%20severity%2C%20and%20increased%20mortality>.

**recovery**

**title:** Pandemic preparedness means policy makers need to work with social scientists

the lancet| 30th may 2022  
  
A multidisciplinary approach is required to understand, address, and recover from pandemics, and social scientific disciplines are central to this. Specialists in anthropology, human geography, and sociology, among other disciplines, generate, interpret, and problematise data about the social world, often directly supporting decision making for public health policies. Importantly, social scientists also challenge and critique policy—practices which are essential for its refinement…  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00983-7/fulltext>

**title:** Future threats from coronaviruses

the lancet respiratory medicine| 23rd may 2022  
  
Global attention is still focused on coronaviruses as the COVID-19 pandemic continues. In a keynote lecture at the European Congress of Clinical Microbiology & Infectious Diseases (ECCMID) 2022, Malik Peiris (The University of Hong Kong, Hong Kong, China) discussed the emergence of coronaviruses and the threats that they pose…  
<https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00191-6/fulltext>

**title:** Prognostic Modeling and Major Dataset Shifts During the COVID-19 Pandemic. What Have We Learned for the Next Pandemic?

jama health forum| 27th may 2022  
  
At the beginning of the COVID-19 pandemic, it was clear that existing recommendations for allocating scarce resources in large disasters were ill-suited for a worldwide respiratory-based pandemic.1 Yet, more than 2 years and 100 published models later, no consensus has emerged on a modeling approach to determine SARS-CoV-2 mortality risk or progression to severe disease. The methodologic shortfalls of these efforts have been well described,2 but there are additional important factors to consider.  
<https://jamanetwork.com/journals/jama-health-forum/fullarticle/2792760>

**title:** Living with covid cannot save lives, but research can

bmj| 30th may 2022  
  
“Research saves lives” and “Data saves lives”— two maxims that have come of age in the past two years of the covid-19 pandemic, not just in the UK, but around the world. Whether this is in terms of development of drugs to treat covid-19 (e.g. the RECOVERY trial and PANORAMIC trial), large-scale surveys of symptoms post-covid (e.g. REACT, ZOE), mechanistic studies to inform vaccination regimes and strategies, or the speed of national data linkage (e.g. OpenSafely, QCOVID, CVD-COVID/COVID IMPACT). Over the past two years, the UK government has frequently asserted that it is “following the science,” but “saved by the science” seems more appropriate.

We are currently following a “Living with covid” approach—an ideology that is difficult, if not impossible, to square with patient safety.1 It is equally hard to see how it “follows the science” and ongoing research into covid-19. It is based on the false premise that we have all the required knowledge, tools, and guidelines to overcome SARS-CoV-2. This complacency is based on falling cases of covid-19 in the UK. But it is worth remembering that surveillance and testing have also reduced. Moreover, it doesn’t take into account the long term and indirect effects on backlogs and waiting lists. The truth is that we do not have all the science, evidence, or care to confidently say that we can “live with covid” in the long term, when we do not know which future variants might arise. We are still learning, and we need to keep enabling the best science and research to happen as quickly as possible…  
<https://www.bmj.com/content/377/bmj.o1361>

**title:** COVID-19 in 2022—The Beginning of the End or the End of the Beginning?

jama|27th MAY 2022

Surveillance. Detection. Response. The elements of a robust public health system to prevent the   
ow in the third year of the coronavirus pandemic, well after the Omicron variant surge, both in the US and globally the number of daily cases had been declining to their lowest levels in more than 6 months. While it seemed that SARS-CoV-2 was moving toward endemicity, US infections are again rising in May 2022, and the reported number of cases is likely a gross underestimate of actual infections because many infections are unreported with increasing at-home testing. Several factors help explain the current trends: The emergence of the BA.2 subvariant of Omicron and the more recently identified subvariant called BA.2.12.1, the limited durability of protection from infection both from vaccination and prior infection, and lifting of mandates (such as mask use) and other restrictions across the country…  
<https://jamanetwork.com/journals/jama/fullarticle/2793011>

**public health & health inequalities**

**title:** Racial and Ethnic Discrepancy in Pulse Oximetry and Delayed Identification of Treatment Eligibility Among Patients With COVID-19

jama internal medicine | 31st may 2022  
  
Question Are there systematic racial and ethnic biases in pulse oximetry among patients with COVID-19, and is there an association between such biases and unrecognized or delayed recognition of eligibility for oxygen threshold–specific therapy?

Findings In this retrospective cohort study of 7126 patients with COVID-19, an analysis of 1216 patients with oxygen saturation levels that were concurrently measured by pulse oximetry and arterial blood gas demonstrated that pulse oximetry overestimated arterial oxygen saturation among Asian, Black, and Hispanic patients compared with White patients. Separately, among 6673 patients with pulse oximetry measurements and available covariate data, predicted overestimation of arterial oxygen saturation levels by pulse oximetry among 1903 patients was associated with a systematic failure to identify Black and Hispanic patients who were qualified to receive COVID-19 therapy and a statistically significant delay in recognizing the guideline-recommended threshold for initiation of therapy.

Meaning The study results suggest that overestimation of arterial oxygen saturation levels by pulse oximetry occurs in patients of racial and ethnic minority groups with COVID-19 and contributes to unrecognized or delayed recognition of eligibility to receive COVID-19 therapies.  
<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2792653>

**title:** COVID-19 boosters and building trust among UK minority ethnic communities

the lancet | 25th may 2022  
  
…In the context of the UK Government shift towards living with COVID-19,7 and the delivery of third and fourth COVID-19 booster vaccinations, it is crucial to recognise that COVID-19 vaccine delivery and uptake are far from fixed or equal. Better understanding is needed about how to support minority ethnic groups and how best the government, health-care providers, and public health teams can work alongside community leaders. This will be vital for promoting public health messaging, openly discussing perceived risks by these groups, and improving health access where there is already deep mistrust, anger, loss, and fear due to structural racism and the inequities these communities have experienced in health care and society.8 However, such understanding will continue to be inhibited by simplistic and homogenising conceptualisations of ethnicity, with a need to recognise the multiple factors that drive both the health and structural inequities in these communities…  
<https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00945-X/fulltext>

**title:** Social media and attitudes towards a COVID-19 vaccination: A systematic review of the literature

the lancet eclinical medicine | 20th may 2022  
  
…Vaccine hesitancy continues to limit global efforts in combatting the COVID-19 pandemic. Emerging research demonstrates the role of social media in disseminating information and potentially influencing people's attitudes towards public health campaigns. This systematic review sought to synthesize the current evidence regarding the potential role of social media in shaping COVID-19 vaccination attitudes, and to explore its potential for shaping public health interventions to address the issue of vaccine hesitancy…  
  
…This thorough examination of the various roles social media can play in disseminating information to the public, as well as how individuals behave on social media in the context of public health events, articulates the potential of social media as a platform of public health intervention to address vaccine hesitancy.  
<https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(22)00184-5/fulltext>

**title:** COVID-19, childhood obesity, and NAFLD: colliding pandemics

the lancet gastroentrology & hepatology | june 2022  
  
…Although COVID-19 inflicted multiple stressors on many families, job losses disproportionately affected already vulnerable communities. School closures were particularly detrimental for children living in poverty, for whom school provides access to healthy food, physical activity, health and social care, social networks, and familiar routines. Similarly, although stay-at-home orders and restrictions on outdoor recreation increased sedentary and screen time for all, children living in densely populated urban areas with no access to green space were particularly affected. Maintaining healthy behaviours requires high personal agency; time; and cognitive, psychological, and material resources that vulnerable families struggled with before the COVID-19 pandemic.5

Since parental stress, mental illness, and disruptions to social environments during childhood are associated with weight gain and obesity in children,7 it is sadly no surprise that this confluence of COVID-19 related stressors has increased childhood obesity prevalence. Hepatologists should be very concerned about these data. An estimated 34% of children living with obesity have NAFLD.4 Although genetic risk influences NAFLD pathogenesis, disease progression is linked closely to obesity, and diet and lifestyle are crucial determinants.8 A population-based study (with data that predated COVID-19) that assessed 4021 24-year-olds by transient elastography with FibroScan suggested that 21% of UK young adults had steatosis.9 Concerningly, 10% of participants had evidence of severe steatosis and 2·7% had evidence of liver fibrosis. Although progression to end-stage liver disease generally takes decades, these data suggest that without lifestyle intervention, there will be a substantial burden of liver disease in 50-year-olds in the near future. The EASL–Lancet Liver Commission has recently proposed a fundamental shift from the management of end-stage liver disease to health promotion, prevention, and early treatment of liver disease.10 The Commission’s call for populationlevel interventions (including policy measures aimed at reducing social inequities and improving the food environment) might seem radical to hepatologists, but is a welcome and timely recognition of long-fought for public health recommendations. The driving question for all of us must be: if these trends in childhood obesity are allowed to continue unchecked, what will the morbidity and life expectancy costs be?  
<https://www.thelancet.com/pdfs/journals/langas/PIIS2468-1253(22)00100-5.pdf>

**international perspectives**

**title:** COVID-19 in the 47 countries of the WHO African region: a modelling analysis of past trends and future patterns

the lancet global health |1st june 2022  
  
…The African region is estimated to have had a similar number of COVID-19 infections to that of the rest of the world, but with fewer deaths. Our model suggests that the current approach to SARS-CoV-2 testing is missing most infections. These results are consistent with findings from representative seroprevalence studies. There is, therefore, a need for surveillance of hospitalisations, comorbidities, and the emergence of new variants of concern, and scale-up of representative seroprevalence studies, as core response strategies.  
<https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00233-9/fulltext>

**title:** The black market for covid-19 antiviral drugs

BMJ |31st may 2022  
  
US hospitals continued to perform eight overused and unnecessary surgical procedures for older   
… A worldwide black market for molnupiravir has developed, despite the drug’s lacklustre results in trials. Although experts now question whether molnupiravir’s approval was premature1 and some doctors eschew its use,2 patients are paying high prices for generic versions online. These drugs are then taken without medical supervision and may not be safe…  
<https://www.bmj.com/content/377/bmj.o1282>

TITLE: COVID-19—HOW EUROPE’S VACCINE DONATIONS WENT TRAGICALLY WRONG

BMJ| 23RD MAY 2022

Covid vaccine equity remains out of reach, as wealthy nations drag their feet on donations, and vaccine stocks pass their use-by dates, write Lucien Hordijk and Priti Patnaik

On 21 December 2021, a truck piled with brown cardboard boxes drove to the Goja rubbish dump in Abuja, Nigeria. Inside the boxes were a million doses of AstraZeneca’s covid-19 vaccine, which were tipped onto the heap, among dirty plastic bags and papers. Two months earlier, Nigeria had agreed to receive 2.6 million doses of the vaccine from the Covax facility, an initiative set up to distribute covid-19 vaccines equitably worldwide. The vaccines, in large part coming from Europe, had been close to expiry. “Some of these vaccines came in with a shelf life of about four weeks,” said Faisal Shaibu, a Nigerian government official tasked with organising vaccination of the country’s 200 million population against covid-19. Following quality inspections and regional allocations, Nigeria administered 1.53 million doses. But the rest were thrown away.

Nigeria, Rwanda, Kenya, and Indonesia have destroyed vaccines received from Europe and North America because they arrived close to expiry.1

According to the pharmaceuticals industry, supply of vaccines is no longer a problem. ‘With almost a billion vaccines now being produced every month, countries’ lack of capacity to vaccinate is now the main barrier to stopping covid-19,” said Thomas Cueni, director general of the International Federation of Pharmaceutical Manufacturers & Associations.2 “It’s scarcity of vaccination, which is due to the lack of country readiness, absorption capacity, and the lack of resources needed to get the vaccines into arms.”

But others say the industry, and donor countries, are shying their responsibilities..  
<https://www.bmj.com/content/377/bmj.o1286>

**title:** The quest for more COVID-19 vaccinations in Africa

the lancet respiratory medicine| 24th may 2022  
  
…Africa has struggled to access COVID-19 vaccines. The vaccine supply picked up by Dec, 2021, after wealthy nations had rolled out booster programmes and had surpluses of vaccines—at which point, more than 80% of people in Africa had not yet received a single dose. Rufaro Samanga, an epidemiologist based in Johannesburg, South Africa, believes this issue of vaccine supply and access is at the heart of the difficulties in trying to increase vaccination rates in Africa. “For the most part, vaccines have been donated to African countries by European and North American countries, which has meant constantly incurring vaccine shortages, having to get rid of vaccines after a short period because of their expiration date, and sometimes simply not receiving the vaccines at all”, she says. “If these donor countries and big pharma companies can disband current proprietary restrictions, more African countries could manufacture their own vaccines. This is more sustainable over the long term”, Samanga adds…  
<https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00193-X/fulltext#:~:text=Africa%20has%20struggled%20to%20access,yet%20received%20a%20single%20dose>.

We

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