this week

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Mental health trust censured over 115 deaths

The Care Quality Commission has warned Norfolk and Suffolk NHS Trust, which provides mental health and learning disability care, that it must improve after 115 unexpected or potentially avoidable deaths were reported between 1 September 2019 and 30 September 2021.

After an inspection last November the CQC reported the trust was failing to ensure patients had up-to-date risk assessments, was not managing long waiting lists effectively, and was failing to ensure staff reported and learnt from incidents to protect patients and staff from harm.

The CQC said child and adolescent mental health wards, community based mental health services for working age adults, acute care wards for working age adults, and psychiatric intensive care units all fell "well short of standards people have a right to expect and were consequently rated inadequate." It identified "severe deterioration" of the trust's inpatient ward for young people who experience an acute mental health disorder, which was previously rated outstanding. This service relied on agency workers and lacked a permanent doctor, and its staff did not have appropriate training to protect young people from avoidable harm, with restraint used too often and incorrectly, CQC said. Staff shortages were identified as a significant factor behind the trust's shortcomings.

The trust was instructed to make a range of improvements, including maintaining safe staffing levels and ensuring training; supervising and appraising staff to support safe, effective care; mitigating all ligature risks and learning from incidents where patients were exposed to harm; and embedding good governance to oversee performance and communicate priorities.

Craig Howarth, head of inspection for mental health and community services at the CQC, said, "If our next inspection finds insufficient improvement, we will take further enforcement action to protect people from the risk of avoidable harm and hold the trust's leaders to account."

Stuart Richardson, the trust's chief executive, apologised for the failure to make progress in some key areas. "We have already taken action that will help us improve, including increasing support and training for our staff, redoubling our efforts to recruit more nurses and doctors, and bringing services closer to people's homes," he said.

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2022;377:o1102

Stuart Richardson, chief executive, has apologised for the lack of progress in key areas at the Norfolk and Suffolk trust

LATEST ONLINE

- Medics demand funding review to stop UK students dropping out because of poverty
- UK-Rwanda migration plan fails to safeguard refugees' medical care, say campaigners
- Obesity: No European country is on track to halt rising levels by 2025, WHO warns

SEVEN DAYS IN

Covid: Discharging vulnerable patients to care homes was irrational, say judges

JONATHAN BRADY/PA/ALAMY

Government policy that exposed thousands of vulnerable elderly people in England to covid in the pandemic's early months was irrational in failing to advise that asymptomatic patients sent to care homes to free up hospital beds should be isolated for 14 days, two senior judges have ruled.

About 20 000 care home residents in England died from covid during the first wave in 2020. Cathy Gardner (far left) and Fay Harris (left), whose fathers were among the deaths, brought a High Court judicial review challenging the lawfulness of early policy.

In March and April 2020 the government published a hospital discharge policy and care home admissions guidance that said that only symptomatic patients needed to isolate. By 2 April, said Lord Justice Bean, with Mr Justice Garnham, there was evidence the virus could be transmitted by asymptomatic carriers, but it was not until two weeks later that both testing and isolation for 14 days were recommended. "The decision to issue the admissions guidance was irrational in that it failed to take into account the risk of asymptomatic transmission, and failed to make an assessment of the balance of risks," the judges ruled.

Clare Dyer, *The BMJ* **Cite this as: *BMJ* 2022;377:o1098**

Reforms

Health and Care Bill receives royal assent

The government's Health and Care Bill received royal assent on 29 April and will now pass into law as the Health and Care Act 2022. The act will put new integrated care systems on a statutory footing. MPs voted against an amendment that would have placed a legal duty on the government to be transparent about the number of staff needed by health and care services in England. But ministers accepted changes to limit new powers given to the health secretary to intervene in decisions over changes to local health services.

Measles

Agencies warn of perfect conditions for outbreaks

The World Health Organization urged countries to get routine immunisation programmes back on track after 17 338 cases of measles were recorded worldwide in the first two months of 2022, up 79% from 9665 cases in the same period of 2021. The relaxation of covid measures, the displacement of millions of people around the world, disruption of routine immunisations, and overcrowding all raise the risk of measles spreading, said WHO and Unicef. Most of the 21 large outbreaks of measles in the past 12 months were in Africa and the eastern Mediterranean.

Prison health

"Urgent action is needed" in Scotland's jails

A report by the Mental Welfare Commission called for urgent action to improve the care and treatment of prisoners in Scotland with mental ill health.

The commission visited all 15 of Scotland's prisons, hearing from staff and prisoners. It examined the experience of segregation, the transfer of very unwell prisoners to hospital, mental healthcare, and addiction to drugs or alcohol. Suzanne McGuinness, executive director of social work at the commission, said, "A joined-up, whole system approach to managing and supporting prisoners and staff across Scotland's prison estate is needed as a matter of urgency."

Research

"Significant rise" in trial reporting in Europe

Over 81% of drug trials that were due to report have made their results available through the European trial registry, data from April 2022 showed—a significant rise from 50% in 2016. Legally, all clinical trials on the European Union Clinical Trials Register must report their results through the register within a year of completion. Despite the progress, however, 19% of due trials—over 3300—are still missing results. The campaigning organisation TranspariMED has warned that these results could be lost forever if they are not made public soon.

Clinical awards

Applications open for reformed awards

The government has invited high performing consultant level doctors, dentists, and academic GPs in England and Wales to apply for the renamed National Clinical Impact Awards. Reforms to the scheme were said to make it "more accessible, inclusive, and fair," particularly for under-represented

groups such as women and ethnic minorities. The government highlighted data from the previous awards scheme showing that in 2020, while 38% of consultants were women, they held just over 21% of awards.

Covid-19

Drug makers urged to share vaccine technology

Campaigners are presenting resolutions at drug companies' annual meetings in an attempt to get them to share technology and knowledge to improve covid vaccine equity. Oxfam America, which has stocks in the companies so it can raise matters of vaccine access, says that 74% of people in high income countries are fully vaccinated but the figure is only 12% in low income countries. Its president, Abby Maxman (left), said, "Moderna, Pfizer, and Johnson & Johnson have prioritised short term profit making over long term sustainability and reputational risks, as well as public health needs."

BIG PICTURE, p 178

MEDICINE

CVD prevention

Expert panel advises against daily aspirin

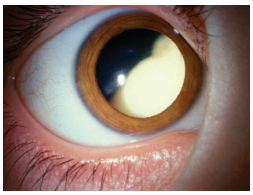
A group of US experts advised against initiating low dose aspirin use for primary prevention of cardiovascular disease in over 60s. The US Preventive Services Task Force said the change to its advice reflected the slightly higher risk of internal bleeding after taking aspirin. For adults aged 40-59 with an estimated 10% or greater 10 year risk of CVD, it added, the decision to initiate low dose aspirin for primary prevention of CVD should be an individual one.

People over 60 have been advised not to start taking low dose aspirin to prevent CVD

Genomic testing

NHS rolls out testing in womb for eye cancer

A test that allows doctors to identify a rare form of eye cancer in babies in the womb is being rolled out by the NHS in England. The non-invasive test, developed at Birmingham Women's and Children's NHS Foundation Trust, can detect changes in the genes in DNA. A blood sample is taken from the mother before birth and tested and analysed for mutations, which can determine with almost 100% accuracy whether the baby will develop retinoblastoma (above), so babies identified as being at risk can be monitored and treated sooner.



General practice

Appointments rose by four million last month

Figures from NHS Digital showed that general practices delivered four million more appointments in March than the previous month. At the same time England has the equivalent of 369 fewer full time, fully qualified GPs than a year ago, the data showed. Kieran Sharrock, deputy chair of the BMA's General Practitioners Committee for England, said this was "completely untenable for practices, for GPs, and for patients . . . This trend, of demand rocketing, while we haemorrhage doctors, is pushing the remaining staff to breaking point."

Asylum seekers

Conditions are unsafe and damage health, says report

Accommodation provided to asylum seekers in the UK does not meet basic standards and is damaging their health, said a report from Doctors of the World and Birmingham University. It identified poor food, a lack of access to sanitary products, and an inability to store medicines or receive health visits among 313 people housed in hotels and former military barracks in 2020 and 2021. The Home Office has rejected the report, claiming that medical support is always available.

Mental health

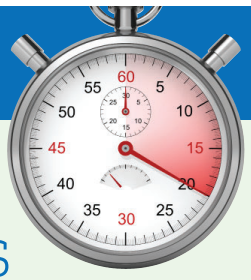
Call for more evidence on effectiveness of apps

The Nuffield Council on Bioethics has called for technologies designed to help people with mental health problems to be appropriately regulated. It called for a better evidence base for devices and virtual reality therapies and said that other treatment options should always be available, as the apps can increase loneliness and isolation.

Cite this as: *BMJ* 2022;377:o1095

BEEF

Replacing **20%** of the beef consumed in the world with microbial protein by 2050 would bring a **56%** reduction in annual deforestation and associated carbon dioxide emissions *[Nature]*



SIXTY SECONDS ON . . . **SUGARY CEREALS**

THEY'RE *GRRREAT*?

Health experts don't agree—and it seems the government is listening. As part of efforts to curb childhood obesity, ministers have tabled legislation in England to restrict the promotion of products high in fat, salt, and sugar.

CEREAL OFFENDERS?

The Department of Health and Social Care says breakfast cereals contribute 7% to children's average daily free sugar intakes, which it described as a "significant amount." But the manufacturer Kellogg's has gone (crunchy) nuts about the move and is taking the government to court.

USING THE *SPECIAL K* DEFENCE?

Not exactly. The company is arguing that the new regulations, which are to come into force in October, fail to consider the nutritional value of the milk added to cereal.

THE RULES ARE LACTOSE INTOLERANT?

Kellogg's points to independent data showing that cereals are eaten with milk or yoghurt in 92% of instances. "We believe the formula being used to measure the nutritional value of breakfast cereals is wrong and not implemented legally," said Chris Silcock, Kellogg's UK managing director.

WHAT DO CAMPAIGNERS SAY?

Caroline Cerny from the Obesity Health Alliance focused more on pouring scorn than milk, calling the claim a "blatant attempt by a multinational food company to wriggle out of vital new regulations." She added, "It's shocking a company like Kellogg's would sue the government over plans to help people be healthier rather than investing in removing sugar from their cereals."

A *FROSTIE* RECEPTION . . .

A court hearing on the matter will start soon, and the government is said to be determined to fight the case amid concerns it might open the floodgates to similar claims from other manufacturers that could undermine the regulations.

FOOD FOR THOUGHT

Indeed. Anna Taylor of the Food Foundation highlighted the £6bn a year the UK spends on treating obesity related conditions and said the new rules were vital to cut this. "This is money we just can't afford to be wasting," she said.

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2022;377:o1097

Cancer patients at greater risk from cost of living crisis, charity warns

Hundreds of thousands of patients with cancer are being forced to put their health at risk because of the UK's cost of living crisis, Macmillan Cancer Support has warned.

With energy and other bills spiralling, 26% of people who are having cancer treatment are having to cut the amount of food they buy, while around one million (32%) are wearing coats indoors to try to stay warm, the charity said. One in six (16%) have been washing their clothes or bedding less—if at all—to keep costs down.

These cuts could harm people's health because good levels of nutrition, warmth, and hygiene were essential to aiding recovery, Macmillan said.

The YouGov survey interviewed 2079 adults who have had a cancer diagnosis, including 222 people undergoing treatment, between 22 February and 13 March. The figures were weighted to represent all people living with cancer. Around 24%, representing an estimated 720 000 people, said they "can't afford life at the moment."

Macmillan research shows that 83% of people with cancer experience some kind of financial impact from their diagnosis. For those affected, this reaches an average of £891 a month, on top of usual expenditure.

The charity said people with cancer who claim the personal independence payment (PIP) were also facing significant delays, an average of 22 weeks, in getting their first payment.

Matthew Limb, London

Cite this as: *BMJ* 2022;377:o1103

Since December nearly a quarter (24%) of people with cancer have had to cut costs either by buying less food or making fewer hot meals, including 26% of those currently having treatment, a poll by Macmillan found

Primary care staff exposed to abuse from patients frustrated at drug shortages

Worsening drug shortages are leaving primary care staff exposed to rising levels of abuse from patients who are frustrated at being unable to access their medication, sector leaders have told *The BMJ*. Longstanding supply chain problems, the effects of Brexit and the pandemic, and high levels of demand have all contributed to shortages.

Many areas of the UK have shortages of HRT, which experts are attributing to sudden increases in demand for oestrogen, particularly transdermal products.

The BMJ has been told that urological drugs and cardiology drugs, among others, are also being affected by supply chain problems that are disrupting practices' work and leaving patients frustrated.

Growing problem

Preeti Shukla, a GP in Lancashire and clinical prescribing policy lead for the BMA's GP committee, told *The BMJ*, "There have been so many shortages. The problem has been growing for a while, but in the past six months it's got worse.

"It's a lot of pressure on GPs and pharmacists, and patients are getting frustrated because they're not getting their drugs on time. It's increasing our workload, and some patients get abusive when they are not getting their medication."

Shukla said the problem was worsening because whole classes of drugs were becoming unavailable, making it difficult to switch patients to alternatives. "Previously it was hard work but we could find an alternative," she said. "Now, there is sometimes nothing available in that class of drug. That has been frustrating for patients and for clinicians, because we have to review the patient again and think about what needs to be prescribed."

Shukla called on NHS England and local commissioners to explain the shortages to patients. "We need a patient facing message to stop the abuse," she said. "If there's a delay, it's not intentional. We're trying to help, but there's a limit to how much we can do, and it's on top of our regular work."

A recent survey of 1132 pharmacy staff and 418 heads of pharmacies by the Pharmaceutical Services Negotiating Committee, which represents community

"Not-fit-for-purpose compensation scheme needs radical overhaul"

MPs have called for a radical overhaul of the NHS compensation scheme in England to remove the need to prove medical negligence.

The Health and Social Care Committee branded the current method of resolving claims through legal action "not fit for purpose" and called for an administrative scheme to replace it. Under the proposals, patients who suffered harm would no longer have to prove that a clinician was negligent but would be compensated if correct procedures were not followed.

The MPs said the system was not only grossly expensive and slow but encouraged a blame culture and discouraged the learning that could help to prevent future errors.

Their wide ranging inquiry examined schemes

Currently a quarter of the enormous taxpayer funded sums ends in the pockets of lawyers
Jeremy Hunt

in New Zealand and Sweden, and those for birth injuries in Japan and the US state of Virginia, which compensate patients quickly and at much lower cost per claim.

The committee's chair, former health secretary Jeremy Hunt, said, "It is unsustainable for the NHS in England to pay out more than £2bn in negligence payments every year—the cost of running four hospitals—a figure that will double in 10 years if left unchecked.

PA

pharmacies in England, heard that 88% deal with shortages every day or several times a week. The Royal Pharmaceutical Society has urged the government to change the law to allow community pharmacists to dispense alternative drugs on prescription without having to contact GPs to alter the script each time.

In response to the HRT supply problems, the health and social care secretary for England, Sajid Javid, issued "serious shortage protocols" on 29 April to limit the dispensing across the whole of the UK of three HRT products to three months' supply. The products are Oestrogel pump pack 750 µg actuation gel, Ovestin 1 mg cream, and Premique low dose 0.3 mg/1.5 mg modified release tablets.

Previously it was hard work but we could find an alternative. Now, there is sometimes nothing available
Preeti Shukla

Gareth Iacobucci, *The BMJ*
Cite this as: *BMJ* 2022;377:o1100

A RECENT SURVEY of 1132 pharmacy staff and 418 heads of pharmacies heard that 88% deal with shortages every day or several times a week

"Under the current system, patients have to fight for compensation, often a bitter, slow, and stressful experience with a quarter of the enormous taxpayer funded sums ending up in the pockets of lawyers."

The report recommended an independent body should initially focus on birth injury claims, which typically cost the most and take years to resolve. If successful, the system should be extended to cover all NHS compensation claims, the report said.

In 2017 the average time from a birth related brain injury to quantifying compensation was 11.5 years. The MPs suggested the new body should be able to provide initial compensation within weeks, with periodic reviews responsive to the child's needs, in place of settlements made once and for all.

The government has promised to create a strategic health authority to investigate serious maternity care incidents. The MPs argued that reconstituting this body, with its independence recognised by the courts, to handle claims and determine eligibility for compensation would be an efficient way to implement the recommendations.

Clare Dyer, *The BMJ*
Cite this as: *BMJ* 2022;377:o1085

Prescribe tailored exercise for osteoarthritis, NICE says

New draft guidance places a greater emphasis on exercise and weight loss in patients with osteoarthritis, with painkillers such as paracetamol and strong opioids not advised.

GPs should offer tailored therapeutic exercise, such as local muscle strengthening and general aerobic fitness, to all people with osteoarthritis, NICE says. Supervised exercise was likely to have greater benefit to people because it may increase adherence and social support.

Long term adherence

Patients should be advised that, although joint pain may increase when they start therapeutic exercise, it will be beneficial, and long term adherence to exercise increases its benefits. Patients who are overweight should also be helped to lose weight and advised that this will improve their quality of life and physical function and reduce pain, says NICE.

The committee agreed that pharmacological treatments may be useful for reducing symptoms and helping people to start therapeutic exercise. However, they should be used at the lowest effective dose for the shortest possible period of time.

Doctors should not routinely offer paracetamol or glucosamine to people with osteoarthritis as there is no strong evidence of benefit. Strong opioids should not be prescribed, as the risks may outweigh the benefits, including possible addiction.

Topical NSAIDs should be the first choice for joint pain, as they are clinically effective in people with knee osteoarthritis and generally the most cost effective drug. If these are ineffective, then an oral NSAID should be considered; however, they can potentially cause gastrointestinal, cardiovascular, and liver and kidney adverse events. Weak opioids should not be routinely prescribed unless for short term relief or if all other pharmacological treatments are contraindicated, not tolerated, or ineffective.

GPs should not routinely offer acupuncture or electrotherapy, but walking aids should be considered for people with lower limb osteoarthritis.

The draft guideline also advises diagnosing osteoarthritis clinically without the need for imaging in people who are over 45, have activity related joint pain, and have either no morning joint related stiffness or morning stiffness that lasts no longer than 30 minutes.

Wendy Holden, Arthritis Action's medical adviser and an honorary consultant rheumatologist at North Hampshire Hospitals NHS Trust, told *The BMJ*, "Most doctors and healthcare professionals have long known that exercise is one of the best forms of medicine, especially for osteoarthritis. Unfortunately many patients with osteoarthritis wrongly still believe that exercise can harm their joints, so they stop exercising and rapidly become deconditioned.

THERAPEUTIC EXERCISE IS BENEFICIAL, AND LONG TERM ADHERENCE TO EXERCISE INCREASES ITS BENEFITS

"These new guidelines are very helpful as they emphasise the importance of self-management for dealing with the pain and stiffness of osteoarthritis, hopefully empowering patients to take control of their symptoms. This advice is likely to be critical, given the now extremely long waits for joint replacement surgery."

Jacqui Wise, Kent
Cite this as: *BMJ* 2022;377:o1099

NEWS ANALYSIS

Stockpiling antivirals for covid risks repeating Tamiflu mistakes, scientists warn

The government has spent more than £2bn on drugs such as Paxlovid to fight covid-19, but some experts are concerned the waste and overspending of the 2000s will recur. **Gareth Iacobucci** reports

The UK government's Antivirals Taskforce has procured more antivirals per population than any other country in Europe, with more than 4.98 million courses ordered so far. This includes 2.75 million courses of Pfizer's oral antiviral drug Paxlovid (a combination of nirmatrelvir and ritonavir tablets).

Andrew Hill, senior visiting research fellow in the Department of Pharmacology and Therapeutics at Liverpool University, has estimated—using publicly available drug prices in the US—that the UK has spent £2.2bn so far on its stockpile. "There's a vast amount of money involved," he told *The BMJ*. "As usual, all government contracts are confidential, so maybe they got some discount. But if the UK paid US prices, which it has with vaccines, then it has spent around £2.2bn on antivirals for covid."

Uncertain evidence

Despite this huge investment, evidence for the effectiveness of antivirals remains uncertain.

Last November Pfizer reported results from an interim analysis of (EPIC-HR) phase 2/3 data showing that Paxlovid, the second oral antiviral drug for covid-19 to be authorised in the UK, can reduce the relative risk of death or hospital admission by 89%. The government used these results to justify its investment. However, the data were based on unvaccinated participants, while most people who would be eligible to receive the drug in the UK have been vaccinated.

Early data indicate that Paxlovid could be more effective than molnupiravir, the first oral antiviral to be made available in the UK, with fewer safety concerns.

The latest rapid recommendation from a WHO Guideline Development Group, published in *The BMJ* last week, strongly recommended Paxlovid for patients with non-severe covid at the highest risk of hospital admission, such as unvaccinated, older, or immunosuppressed patients. But it made no recommendation for patients with severe or critical covid-19, as there are no trial data on Paxlovid for this group. Both studies that informed the recommendation (EPIC-SR and EPIC-HR) excluded patients with severe or critical illness, and all patients were unvaccinated.

The Panoramic trial

The UK's large national Panoramic study, run by Oxford University in collaboration with hubs of general practices, is aiming to fill the gaps in the evidence base by assessing how antivirals work when most of the adult population is vaccinated.

For several months, Paxlovid has been available directly through the NHS to a limited number of people at higher risk of serious illness who test positive for SARS-CoV-2, including those who are immunocompromised, patients with cancer, and people with Down's syndrome. This month Paxlovid was added to the Panoramic study and will be offered to 17 500 vulnerable people in England, in addition to the 23 000 previously recruited to receive molnupiravir.

Nick Lemoine, medical director at the National Institute for Health and Care Research, which is funding the study, said, "While smaller scale studies have already shown this new antiviral treatment to be highly effective against covid in the early stages of infection, additional evidence from much larger cohorts is needed to enable clinicians and health

Evidence from much larger cohorts is needed
Nick Lemoine

How do you justify spending a 10th of the NHS drug budget on drugs that might not work?
Andrew Hill

services to make best use of these exciting new treatments."

Some experts fear ministers have jumped the gun by stockpiling when the evidence is still uncertain. Hill said, "If the drug fails in Panoramic, can the UK get the money back? And how do you justify spending a 10th of the entire NHS drug budget on drugs that might not work at all?

"I think there are a lot of parallels with Tamiflu, and it could be a repeat. With Tamiflu [and Relenza] the government wasted £600m. This time we're talking £2.2bn."

In a recent editorial published in *The BMJ*, James Brophy, professor of medicine and epidemiology at McGill University, Montreal, argued that molnupiravir was authorised for covid patients without sufficient evidence. He told *The BMJ* that although the situation was less clear cut with Paxlovid he held similar concerns. "There is so much uncertainty as to what is the effect size [in the EPIC-SR trial], especially in vaccinated people," he said.

Brophy attributes the early stockpiling to what he bluntly calls a "'cover our ass' mentality, which says, 'Let's look like we are doing something even if we aren't sure it works and it costs a fortune, since we don't want to be criticised.'"

The Department of Health, when asked whether it would be able to recoup any of the money spent on procuring Paxlovid if the drug was shown not to be effective, said that details on costs and the recuperation of drugs were commercially sensitive. A spokesperson added, "We have secured more lifesaving antivirals per head than any other country in Europe for NHS patients, and we make no apologies for doing so.

"Both antivirals have been shown to be highly effective in clinical trials, as well as by our medicines regulator. For example, Paxlovid reduced the relative risk of hospitalisation or death due to covid by 88%. The Panoramic study is collecting further data on how antivirals work in a vaccinated population, to inform the wider rollout later this year."

Low uptake

Aside from the evidence, it is also becoming apparent that supply of antivirals is exceeding demand, casting further doubt on the wisdom of stockpiling them.

Uptake in the UK is modest. NHS England said that around 32 000 patients had received antivirals since December, when they were introduced for people outside hospitals, and that only around 6000 had received Paxlovid as of 9 April. An analysis by Reuters showed that supply of Paxlovid has far outstripped demand in the UK, the US, Japan, and South Korea. Complex eligibility requirements, reduced availability of testing, and potential for drug interactions have all been cited as potential barriers.

Hill noted that the need to administer Paxlovid swiftly after infection was a major practical hurdle. "You have to start treating within five days of the symptoms first appearing," he said. "You get a lot of people who don't know if it's actually covid on the first day. Then you've got to get a test, then you've got to get a GP appointment at short notice, and then get a prescription. I'd suggest this is very hard for most people."

He added, "The other very serious issue with this drug is that it could cause more harm than good. It contains a booster drug called ritonavir, which causes drug interactions by increasing the concentrations of other drugs. For that not to happen, somebody has to have a very detailed review of all the patient's comedications, which could take ages."

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2022;377:o1053

FABIAN SOMMER/DPA/ALAMY

BRIEFING

What is the evidence for Paxlovid in covid-19?

Andy Extance reports on Pfizer's combination antiviral treatment that is moving from the laboratory to patients around the world at record speed

What is it?

Paxlovid is an antiviral combination developed by the pharmaceutical giant Pfizer. The treatment includes the newly developed antiviral drug nirmatrelvir and ritonavir, a potent inhibitor of the cytochrome P450-3A4 (CYP3A4) enzyme that metabolises several classes of drugs. Ritonavir slows down nirmatrelvir's breakdown, thereby increasing drug concentrations and delaying clearance.

Patients take Paxlovid as three tablets, two 150 mg tablets of nirmatrelvir and one 100 mg of ritonavir together, twice daily for five days. As with the covid antiviral treatment molnupiravir, the oral route of delivery makes it convenient to take at home, unlike some other drugs for covid, which require intravenous infusion.

Who is eligible for treatment?

It is authorised for people older than 12, weighing more than 40 kg, who have mild to moderate covid-19, and who are at high risk of progression to severe symptoms, hospital admission, or death. Treatment should start as soon as possible after diagnosis and within five days of the onset of symptoms.

On 9 March this year Pfizer started a phase 2/3 trial in 140 children aged 18 or younger.

Pfizer, which has its headquarters in New York (far right), began trials of Paxlovid (right) in 2020. It was authorised for use in the UK, US, and elsewhere less than a year later

It leaves the virus unable to make any functional proteins and therefore unable to replicate

How does Paxlovid work?

When SARS-CoV-2 RNA enters an infected cell, it uses its host's translational machinery to make the proteins needed for the virus to function and assemble new copies of itself. That machinery translates the virus genome into two large polyproteins, which two protease enzymes then cut up into smaller pieces.

One of them is SARS-CoV-2's main polyprotein protease enzyme, SARS-CoV-2 Mpro. Nirmatrelvir blocks SARS-CoV-2 Mpro, so that it can't bind the polyprotein. That leaves the virus unable to make any functional proteins and therefore unable to replicate. SARS-CoV-2 Mpro is unlike any human protease, which should limit the drug's toxicity.

Nirmatrelvir originated from a Pfizer research programme into the original SARS in 2002. That led to an intravenous preclinical candidate, PF-00835231, which worked well against SARS-CoV-2. Starting in February 2020, Pfizer sought to adapt this into a drug that could work orally. In one week in July 2020 the company's scientists prepared 20 drug candidates, of which nirmatrelvir was one.

Ritonavir is also a protease inhibitor originally developed to treat HIV-1 infections. In Paxlovid, it inhibits nirmatrelvir breakdown in the liver so that it reaches higher concentrations and is eliminated more slowly. The effect of ritonavir on P450 can be a problem if patients are taking other drugs that this enzyme breaks down. These include anticoagulants, anticonvulsants, corticosteroids, pethidine, amiodarone, flecainide, colchicine, clozapine, lovastatin, simvastatin, sildenafil, and midazolam.

What peer reviewed evidence is there?

While nirmatrelvir was designed specifically to target SARS-CoV-2 Mpro, in vitro analysis showed it stopped SARS-CoV-1, SARS-CoV-2, MERS, and 229e coronaviruses affecting cells. It also protected mice against SARS-CoV-2 when taken orally. By the time those results were published, Pfizer had already completed a phase 1 clinical trial in healthy participants and started a phase 2/3 trial, called EPIC-HR, for covid.

The phase 1 trial studied nirmatrelvir as a single agent and also in combination with ritonavir. Finding that drug concentrations remained higher for longer in the combination, Pfizer used it in EPIC-HR, which randomised 2246 patients, with 1120 receiving 300 mg of nirmatrelvir and 100 mg of ritonavir and 1126 receiving placebo twice daily for five days.

On 5 November 2021 Pfizer announced an interim analysis of 774 patients who were treated within three days of symptom onset. Just three of 389 patients (0.77%) who received Paxlovid had been admitted to hospital by day 28. Twenty of 385 patients taking placebo had been admitted in this time, and a further seven had died; those 27 people comprising 7% of the placebo group.

Pfizer announced the final data on 14 December, publishing them in the *New England Journal of Medicine* on 16 February. The primary analysis again looked at patients who had received Paxlovid within three days of symptom onset. Five of 697 patients (0.72%) receiving Paxlovid had been admitted to hospital by day 28. In the placebo group, 35 of 682 patients had been admitted in this time, and a further

MELVYN LONGHURST/ALAMY

Paxlovid should be used as part of a strategy for vaccination, testing, and rapid treatment for patients at higher risk
Steve Pearson

nine had died, those 44 people comprising 6.45% of the placebo group.

When the analysis was extended to people who received Paxlovid within five days of symptom onset, the data showed that eight of 1039 patients (0.77%) in the Paxlovid group and 66 of 1046 (6.31%) in the placebo group had been admitted to hospital with covid or died from any cause through to day 28. The consistency between the interim and the final analysis contrasts with molnupiravir, whose full study results were worse than those its developers initially stated in a press release.

Although three are not yet peer reviewed, this January Pfizer publicised four BioRxiv preprints regarding effectiveness of Paxlovid against the covid-19 variants of concern, including omicron. One preprint showed that Paxlovid retained its efficacy against variants and another showed why. Two further studies also showed that Paxlovid, remdesivir, and molnupiravir all retained their activity against such variants, one of which has now been peer reviewed and published in *Antiviral Research*.

Which countries are using the drug?

Pfizer sought emergency use authorisation for Paxlovid from the US Food and Drug Administration 11 days after press releasing its interim analysis, on 16 November 2021. It received that authorisation on 22 December, less than a year after the first patient received the drug in clinical trials and only two years after the pandemic began. Scientists have hailed this as the fastest drug development project on record.

Israel's health ministry approved Paxlovid on 26 December 2021, as did the UK's Medicines and Healthcare Products Regulatory Agency on 31 December. The European Medicines Agency recommended conditional marketing authorisation on 27 January 2022. And on 11 February China's National Medical Products Administration granted Paxlovid emergency approval, the first foreign drug or vaccine the country had approved for covid-19.

On 17 March the United Nations backed Medicines Patent Pool signed agreements with 35 manufacturers of generic drugs in Europe, Asia, and Central and South America to make Paxlovid and supply it to 95 poorer countries. Then, on 22 March Pfizer agreed with Unicef to supply four million courses of treatment to 95 low and middle income countries, pending authorisation or approval, beginning in April 2022. Two days later, the Africa Centres for Disease Control and Prevention agreed to a memorandum of understanding with Pfizer to provide Paxlovid for African countries. However, availability in India of a locally made generic version of Paxlovid has been held up by a requirement of the country's Central Drugs Standard Control Organisation for extra trials.

At the time of writing, the World Health Organization's assessment of nirmatrelvir and ritonavir combination therapy was ongoing, a spokesperson told *The BMJ*.

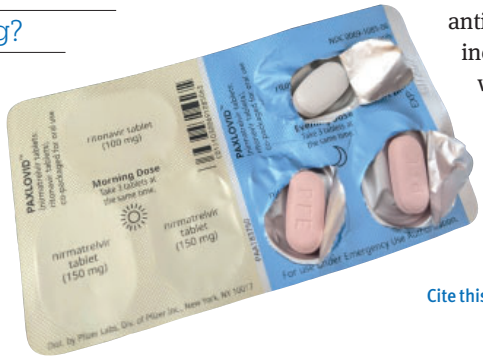
How much does it cost?

In the US, a five day course costs $529 (£410; €490), according to the independent US non-profit Institute for Clinical and Economic Review. It estimated that this equated to $21 000 per hospital admission averted in that country.

What's the potential for this drug?

Paxlovid should be used "as part of a comprehensive strategy for vaccination, testing, and rapid treatment for patients at higher risk of progressing to more serious covid-19," Steve Pearson, president of the Institute for Clinical and Economic Review, told *The BMJ*. "The key feature of the oral treatments is that they may help make administration of rapid treatment more feasible across different types of healthcare settings," he added.

Like any antimicrobial drug, including antibiotics, relying too heavily on Paxlovid increases the chances that SARS-CoV-2 will evolve to become resistant. WHO's spokesperson agreed, saying, "Prevention is better than cure. Even if proved safe and effective, antiviral drugs will not be alternatives to vaccines."



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THE BIG PICTURE

Campaign takes on Pfizer "profiteering"

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) in 2021, it has contributed to a 15 billion dose gap in global supplies needed for 2022.

WHO has also named Pfizer among the drug companies which it believes should be doing more to improve covid vaccine equity and access.

In response to the claims Pfizer said it was "firmly committed to equitable and affordable access to the Pfizer-BioNTech covid-19 vaccine to help bring an end to the pandemic for everyone, everywhere.

"As of 3 April nearly 3.3 billion Pfizer-BioNTech vaccines have been shipped to 179 countries in every region of the world."

Alison Shepherd, *The BMJ*

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JESS HURD/GLOBAL JUSTICE NOW

EDITORIAL

A long term workforce plan for the English NHS

The health system desperately needs one, but—so far—government has failed to deliver

Pressures on the English NHS are extreme. In March 2022, 22 500 people waited more than 12 hours on trolleys in emergency departments for a hospital bed—32 times more than March last year and 68 times more than before the pandemic in 2019.[1] More than six million people are waiting for routine hospital treatment, and 300 000 have waited more than a year.[2] The healthcare system is buckling under the strain, and patients and staff are suffering as a result.

A mix of factors are to blame: a decade of underinvestment in the NHS, limited hospital capacity, massive disruption from covid-19, political neglect of social care, and more. But chronic workforce shortages are probably the biggest issue facing the NHS and its patients.

NHS staffing gaps currently stand at around 110 000[3] and could grow substantially higher by 2030.[4] The UK has fewer doctors and nurses per capita than most comparable countries.[5]

Staff absences

Covid-19 has made things worse. Around 70 000 hospital staff were off sick or self-isolating at the start of April 2022—29 000 because of covid-19.[6] And more staff will now be needed to tackle the growing backlog of unmet healthcare need. Recent estimates suggest an extra 6200 consultants and 25 700 nurses will be needed over and above existing NHS staff vacancies to meet government targets for elective care by the end of the parliament.[7]

The picture is no better outside hospitals. The number of general practice appointments is now higher than before the pandemic, but numbers of permanent, fully qualified GPs have fallen since 2016.[8] These pressures are not evenly distributed, with fewer GPs per patient in more deprived areas.[9]

DAVID GROSSMAN/ ALAMY

Staffing shortages are an existential threat to the future of the NHS

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Workforce gaps in the NHS also interact with shortages in social care, where staff vacancies are estimated at around 105 000.[10] Staffing levels affect quality of care and access to services,[11 12] and insufficient staffing was one of the issues highlighted by Donna Ockenden in her recent review of maternity services at Shrewsbury and Telford NHS Trust.[13]

None of this is a secret. In the 2021 NHS staff survey,[14] only around 27% of staff said that there were enough staff in their organisation for them to do their job properly—down 11 percentage points since 2020.

The public know it too. Public satisfaction with the NHS dropped substantially in 2021, falling to its lowest levels since the 1990s.[15] The NHS not having enough staff was among the top reasons for people's dissatisfaction, along with long waiting times and lack of investment—both linked to staffing.

Inaction

Yet—incredibly—government has not grasped the scale of the problem. A comprehensive and long term approach is needed. But government has not produced a detailed plan for reducing chronic staff shortages. The Treasury has repeatedly failed to provide enough long term funding to train and develop the future workforce.[18] And government has, so far, blocked a proposed amendment to NHS legislation currently being debated in parliament to ensure independent projections of future workforce needs are produced and published to support policy decisions.

The prescription is clear: the NHS needs a long term workforce strategy, backed by sustained investment. The task is complex. The strategy must assess how many staff of which type may be needed in future and how they will be trained, recruited, and retained once they are in the NHS. This means considering how care may change to meet people's health needs, as well as how to reduce staff workload and improve organisational culture. There are no magic bullets, and a combination of policy changes will be required—including to boost domestic training and ethical international recruitment, develop more team based care, distribute staff equitably between areas, and ensure staff are fairly rewarded.[19] And—ultimately—the Treasury must be convinced to fund it. A similar strategy is needed for social care too.

In a speech on health reform earlier this year, the health secretary promised a "proper long term workforce plan" for the NHS.[20] But this has been promised for several years, and only short term measures have materialised. The health secretary also said that no extra money would be provided to fund the new plan.[21] So it is unclear what will be different this time around. Another short term fix would be a disaster for the NHS and its patients—and would hold back efforts to reduce waiting lists and improve services. Staffing shortages are an existential threat to the future of the NHS. Government must get serious about fixing them.

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EDITORIAL

A roadmap towards a healthy data-centric NHS

The Goldacre report successfully takes up a timely challenge

Tasked by the UK government with daring terms of reference, the Goldacre report, published on 7 April, draws the UK's roadmap towards "better, broader, and safer" use of health data for research and analysis.

Because raw data are not powerful on their own, they must be skilfully curated, securely managed, properly analysed, openly communicated, and responsibly acted on.[1] To this end, the authors carefully examine the technical, ethical, and organisational issues associated with health data and recommend that we consolidate "trusted research environments," professionalise the data analytics workforce, operationalise ethical principles, and avoid common misconceptions about "open" data analytics.

In the US, when Google and the University of Chicago Medical Center were sued for violating patient privacy, the media raised concerns about "health systems sharing data with big tech."[2] Large scale biobanks and genetic data repositories raised similar public controversies decades earlier.[3] Whether research institutions could "be trusted to handle data ethically" was called into question, as they were unable to account for storage, sharing, linkage, and re-use of data.[3]

Today, debates on digital health data often focus on patient consent and neglect fundamental public policy questions, such as ways to establish a fair distribution of the benefits and burdens across stakeholders.[2]

The Goldacre report rightfully calls for "frank public conversations about commercial use of NHS data."[1] Because the "track record of big data driven innovations in healthcare is decidedly mixed" and their health benefits have not yet been assessed rigorously,[2] public policies are required that can account for the common good embedded in health data created through public resources.[4]

MARK THOMAS

Major public works lie ahead to bring the NHS and its digital infrastructures, and competences into the 21st century

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Carbon footprint

Data exploitation, at the scale described in the Goldacre report, comes at a high environmental cost. As technical solutions rely on energy and resource intensive hardware and software, it's intriguing that none of the 12 questions underlying the report's terms of reference consider the carbon footprint of health data and analytics.

With the overall digital carbon footprint increasing by 8% a year,[5] rich countries—where digital consumption is the highest—hold specific responsibilities towards low and middle income countries that are disproportionately affected by climate change.[6] The health consequences of growing digital healthcare and analytics on people and the planet cannot be ignored.

The NHS is an international leader in environmental sustainability, but links between wanting to harness data to improve healthcare and the harm caused by expansive digitalisation are rarely made.[8] For anyone who still considers the digital as intangible, Kate Crawford's *Atlas of AI* is a must read.[4] Primary care providers who are committed to harm prevention and patient health across the life course[9] might agree that the "only appropriate response" to the latest report of the Intergovernmental Panel on Climate Change is "immediate, unequivocal action."[10]

The perceived double burden of caring for patients and caring for the planet must be transformed into a single duty of care.[11] For NHS data to truly "save lives around the world," [1] digital healthcare—from data collection to advanced analytics—must now be built using "digital sobriety."[5]

Where do we go from here?

Policy makers worldwide will find the Goldacre report to be insightful and relevant and to contain readily transferable recommendations, including professionalising the work of data analysts and ceasing to impose low value data collection tasks on healthcare workers.

The report lays out the comprehensive vision and practical knowledge that many governments wish they had had in the 1990s when computerised medical records and telehealth were emerging. It recognises that major public works lie ahead to bring the NHS and its digital infrastructures, skills, and competences into the 21st century.[1]

To align such public works to meet current global health challenges, it would be wise to reward the development of more responsible, sustainable, and inclusive digital infrastructures.[8 12] The need for transparent and accurate data on the carbon footprint of health data and analytics is clear.[5] Knowing that discussing climate action in terms of health has proved to be an effective communication strategy to help patients and health professionals conceptualise climate change as salient to their lives,[9] the NHS has much to offer to other countries.

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FEATURE

From Ukraine to remote robotics: how videoconferencing and next generation technology are transforming surgery

As surgeons in Ukraine respond to the challenges of war with the help of teaching and learning through Zoom, **Jo Best** discovers how digital technology will continue to change the face of surgery around the world—and the challenges that still have to be to overcome

When Russia's invasion of Ukraine began in February, medics and surgeons from across Europe and beyond reached out to support their colleagues in the country. As well as answering calls for equipment and resources for combat injuries, surgeons from outside Ukraine turned to videoconferencing platforms such as Zoom to share expertise with doctors caught up in the conflict.

Henry Marsh, a British-born neurosurgeon and author who has been operating in Ukraine since the 1990s, was one of the surgeons offering advice over Zoom.

While 25% of battlefield deaths are because of head injuries, "the actual acute management of head injuries in a war zone is limited. You don't carry out major brain surgery," Marsh told a Royal Society of Medicine event in April. "If somebody comes in in a coma with a penetrating injury, you triage them to have no treatment.

"What neurosurgery is done in a battlefield is non-urgent, it's done within 24 hours to repair superficial open injuries. It's very different from civilian practice."

From webinar translation to bunker

Marsh's Zoom discussions with Ukrainian doctors were part of a March webinar arranged by the David Nott Foundation, an organisation set up by the eponymous surgeon to train doctors in conflict affected areas.

The course was a condensed version of the foundation's five day Hostile Environment Surgical Training programme. The webinar, attended by more than 570 Ukrainian doctors, aimed to provide a crash course on how to deal with war injuries across subjects including burns, plastics, triage, and damage control.

The foundation established by David Nott (right) arranged the conflict surgery webinar sessions carried out by Henry Marsh (left)

In the weeks that followed the invasion, the European surgical not-for-profit AO Foundation also ran sessions for doctors over Zoom. The sessions were set up after discussions with AO's Ukrainian chair. "He explained that Ukrainian surgeons are not experienced in treating the kinds of war injuries they were now facing," Anja Sutter, senior project manager events and relations at the foundation, tells *The BMJ*.

Some of the Zoom sessions were attended by hundreds of doctors at a time, and continued even in difficult circumstances. "Sometimes our translator, a faculty member from AO Trauma Ukraine, had to go to a bunker because of a bomb alarm during a live session and another faculty had to take over for a time," Sutter says.

Ukrainian Zoom sessions were attended by hundreds of doctors at a time

The sessions focused on dealing with war injury and trauma, with surgeons from eight countries contributing to more than 40 hours of teaching. Recordings of the sessions remain available on the AO website for doctors to access whenever they need to.

Defining and refining the advice

Mansoor Khan, a consultant surgeon with extensive experience in war zones, says that, as conflicts evolve, the surgical support that is provided online needs to be tightly focused on the needs of those on the ground. "The first thing you have to ask is, what do you need, in terms of education and resources?" he tells *The BMJ*.

"These guys are seasoned surgeons. Ukraine's been in conflict with Russia for a number of years now, so they've got experience. What we need to try and find out is what they require, not what we think they need to learn."

At the start of the conflict, doctors outside Ukraine used videoconferencing platforms as a way of sharing broad based knowledge with as many of their colleagues in the country as possible. Now, surgeons in Ukraine are also using other digital tools to get advice on complex cases.

"Telemedicine is not only about showing people what to do, it's also using tools like WhatsApp," Khan says. Through such messaging services, European surgeons are now doing quick case reviews and giving highly targeted advice to their Ukrainian colleagues. "Within three sentences, you can give them a plan."

NEIL WEBB

What neurosurgery is done in a battlefield is non-urgent
Henry Marsh

These guys in Ukraine are seasoned surgeons
Mansoor Khan

It enables teaching and training to become more accessible to many more people
Richard Kerr

Existing technology, future learning

Using videoconferencing to support doctors overseas, or in areas with increased need or low resources, is not new. Médecins Sans Frontières uses secure videoconferencing for clinical case discussions, clinical supervision, patient consultations, and training, for example.

Throughout the pandemic, UK surgeons have been using platforms such as Zoom and Teams to keep up with colleagues for teaching, conferences, collaboration, and team meetings. The spread of videoconferencing and its ability to support geographically dispersed teams could mean teaching and learning nationally and internationally could play a greater role in surgical practice in future.

"It enables teaching and training to become more accessible to many more people," says Richard Kerr, consultant neurosurgeon and council member of the Royal College of Surgeons of England. "Even in this country, part of the medical curriculum is seeing and being exposed to surgical procedures. You can imagine a time when two or three units will club together, so trainees can see what's happening in the other units. They can dial in to operations when there may be surgeons that are doing particular procedures.

"This is going to increase the exposure, and therefore the experience, of trainees."

Improving caesarean section safety in Kenya

Several new digital platforms aim to build on traditional videoconferencing to allow surgeons to collaborate on cases in real time with functionality that replicates hands-on practice.

Proximie, which combines videoconferencing with technologies such as augmented reality, enables surgeons in one location to see many views of a theatre in another. They can mark up patients and give input in real time as the case progresses.

In Makueni county, Kenya, a project is under way to use this technology to improve the safety of caesarean sections. The county, which has a population of more than 900 000, has just three obstetrics and gynaecology consultants working across two hospitals, with most sections performed by junior doctors known as medical officers.

As part of the Obstetric Safe Surgery project, supported by organisations including Johns Hopkins University affiliate Jhpiego, Proximie technology has been rolled out to five hospitals in the county with the aim of improving maternal and newborn outcomes.

Using the technology, consultants mentor medical officers through simulated caesarean sections, as well as provide training on infection prevention, use of the World Health Organization's surgical safety checklist, administration of anaesthesia, and care of newborns immediately after delivery.

Patients will need to be convinced of the privacy of the technology

The consultants are also starting to assist remotely with elective cases, with Proximie using four views of the theatre—the entire theatre, the operation site, anaesthesia, and the infant resuscitation area—to give an overview of the operation as it happens. Those watching remotely can annotate and highlight areas of the surgical field for those in the theatre.

Privacy, scheduling, and connectivity concerns

Before the technology can be used more widely, there are problems to overcome. Patients will need to be convinced of the privacy of the technology. Doris Mbithi, medical superintendent of the Mother and Child Hospital in Makueni county and one of its consultants, notes that some patients are concerned footage will end up on the internet.

And setting up a session, which must be scheduled in advance by an IT specialist, will need to be made quicker and simpler. Broadband connectivity is also a problem. "That has been our main challenge," Mbithi says. "Sometimes you schedule a live case and the consultant joining virtually is not able to continue guiding because the internet keeps disconnecting."

Within the coming months—assuming these challenges can be overcome—the technology will progress from being used for training to allowing consultants to advise on emergency cases happening in facilities hours away. "It's a good technology for mentorship. It's my wish that it can also work for emergency cases where a surgeon is stuck in a small facility and then you can log in and assist them to save a life," Mbithi says.

The Proximie project allows consultants to follow procedures carried out in hospitals in Makueni, Kenya

Telesurgery hopes and challenges

In the future it's likely that remote surgical collaboration technology will evolve to the point where surgeons in one location use surgical robots to operate on patients in another. A handful of such remote surgeries have already been performed on cadavers, animal models, and humans, including the reported insertion of a deep brain stimulator in a patient with Parkinson's disease by a surgeon controlling a robotic arm from a city 3000 km away.

The spread of such remote telesurgery will depend on the uptake of two technologies: surgical robotics and 5G networks. Such mobile networks will reduce latency—the delay between when data are sent and received—to under 1 millisecond. At the same time, it will increase download speeds to a theoretical peak of over 1 gigabit per second. Both are notable steps up from what is currently available through 4G networks and are necessary to allow the surgeon and robot to operate in an as near real time environment as possible, without any lag between the surgeon's and the robot's movements.

The hope is that telesurgery will eventually allow hospitals in remote or low resource areas access to surgeons from elsewhere to perform operations. It is, however, a promise not set to be realised in the short term. Of those 5G networks currently up and running, only a small percentage are in developing areas, and the vast majority of 5G networks worldwide are not of the type that could support remote surgery, according to Jason Leigh, manager of 5G and mobility research at technology analysts IDC. "The areas that could most benefit from surgical virtual reality support and robotic telesurgery are also those that are lagging in 5G deployment."

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