

this week

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Hancock bars extra legal cover for doctors

England's health secretary has rejected a call to bring in emergency legislation to protect doctors from "inappropriate" legal action amid fears that the NHS will be overwhelmed by the covid-19 pandemic.

Doctors are worried that not only will they be forced to choose which patients to treat but they could be vulnerable to a criminal investigation should a patient die in such circumstances. Their fears follow a warning on 6 January that hospitals were less than two weeks from being overwhelmed.

The doctors' plea for emergency legislation came in a letter to Matt Hancock, signed by seven organisations, including the Medical Protection Society, BMA, Doctors' Association UK, Hospital Consultants and Specialists Association, and the British Association of Physicians of Indian Origin.

The letter said that guidance available to doctors on administering and withdrawing treatment does not provide legal protection and does not consider covid-19 specific factors such as surges in demand for resources temporarily exceeding supply. It added that health professionals should not "suffer from the moral injury and long-term psychological damage that could result from having to make decisions on how limited resources are allocated, while at

the same time feel vulnerable to the risk of prosecution for unlawful killing."

NHS doctors are covered by state indemnity for clinical negligence and by an additional scheme that covers pandemic responses. The GMC has also said the covid context will be taken into account when it considers complaints. But the groups' letter said they did not address their concerns.

Asked by *The BMJ* about the letter, Hancock said intensive care capacity was a "very serious concern." But he added, "I am very glad to say we are not in a position that doctors have to make these sorts of choices and very much hope that we don't get into that situation. It is not necessary at this point to change the law on this matter."

A day later, on 19 January, the Royal London Hospital reported that all its ICU beds—recently expanded from 44 to 150—were occupied.

Jane Dacre, president of the Medical Protection Society, was disappointed with Hancock's response. "Healthcare staff need this legal protection now. It would enable doctors to focus on doing the best for their patients without fear of unfair investigations," she said.

Clare Dyer, *The BMJ*

Cite this as: *BMJ* 2021;372:n164

With the threat of ICUs being overwhelmed, doctors fear being subjected to criminal investigations if a care decision based on resources leads to a patient's death

LATEST ONLINE

- Spain to become the sixth country to allow euthanasia and assisted suicide
- What covid variants are emerging, and how are they being investigated?
- Government using lateral flow tests to keep children in schools against regulator's advice



SEVEN DAYS IN



NEIL HALL/PA

Doctors' leaders call for revised PPE guidance

Medical leaders have urged Public Health England to strengthen its guidance on personal protective equipment to reflect the more transmissible forms of SARS-CoV-2.

Current guidance says that higher grade FFP3 masks should be provided to staff who are involved in aerosol generating procedures, but other staff looking after patients with covid-19 are only required to wear fluid resistant surgical masks.

In a letter to PHE sent on 13 January, BMA council chair Chaand Nagpaul said that, in light of the new variant of SARS-CoV-2, increased spread of the virus, and growing evidence of aerosol transmission, it should review its recommendations on PPE usage "so that a more precautionary approach is adopted to the provision of respiratory protective equipment (RPE) to ensure staff are protected from aerosol transmission."

He wrote: "There are significant and growing concerns about the role of aerosol transmission of covid-19 in healthcare settings, and the need for wider use of RPE (for example, FFP3 respirators) outside of those procedures designated as aerosol generating. We are therefore calling on [PHE] to support the wider use of RPE in other high risk settings across primary and secondary care."

Gareth Iacobucci, *The BMJ* Cite this as: *BMJ* 2021;372:n146

Covid-19

Many ICU staff in England report PTSD

Nearly half of 700 intensive care and anaesthetic staff surveyed in six English hospitals last June and July reported symptoms consistent with a probable diagnosis of post-traumatic stress disorder (PTSD), severe depression, anxiety, or problem drinking. The preprint, from researchers at King's College London, also reported that 13.4% of respondents had had thoughts that they would be better off dead or of hurting themselves. The BMA's mental health lead, Andrew Molodynski, said that a supportive workplace culture and high quality wellbeing support were vital.

Trials needed into convalescent plasma

An observational study in the *New England Journal of Medicine* found that convalescent plasma seemed to be of most benefit to patients who received transfusions containing high levels of antibodies early in the course of covid infection. Death within 30 days of transfusion occurred in 22.3% of the high titre group, as compared with 29.6% in the low titre group. Experts say that results of randomised

trials are necessary to know whether convalescent plasma is beneficial. One such trial from India, published in *The BMJ* in November, found that it did not reduce disease progression or mortality from all causes.

Japan's suicide rate falls then rises

Monthly suicide rates in Japan declined by 14% in the first five months of the pandemic (February to June 2020) but increased by 16% in the second wave (July to October), showed a study published in *Nature Human Behaviour* that covered Japan's entire population of 120 million. It found that suicide rates rose the most among women (up 37%) and children and adolescents (up 49%). The authors argue that the results are consistent with other studies showing the crisis disproportionately affected female dominant industries and that stay-at-home orders magnified mothers' burdens.

Skin rash is present in 17% of positive covid cases

Researchers from King's College London compiled a catalogue of images of the most common skin manifestations of covid-19

(<https://covidskinsigns.com>) after finding an association between skin rashes and a



positive swab test result (odds ratio 1.67 (95% confidence interval 1.41 to 1.96)), from data on 336 847 UK users of the Covid Symptom Study app. Reporting in the *British Journal of Dermatology*, they also found that among 11 546 survey respondents 17% of SARS-CoV-2 positive cases reported skin rashes as the first presentation and 21% as the only covid-19 clinical sign.

Inequalities

NHS Race and Health Observatory board named

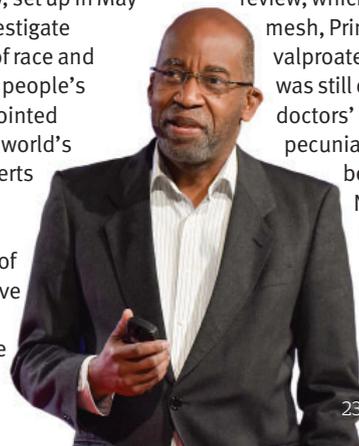
The NHS Race and Health Observatory, set up in May 2020 to investigate the effects of race and ethnicity on people's health, appointed some of the world's leading experts on health inequalities to its board of non-executive directors. They include

David Williams (below) of the Harvard School of Public Health; Michael Marmot of the UCL Institute of Health Equity; Donna Kinnair, chief executive of the Royal College of Nursing; Kevin Fenton, London regional director for Public Health England; and Chaand Nagpaul, chair of council at the BMA.

Patient safety

Government will appoint commissioner in England

The government plans to appoint a patient safety commissioner to oversee healthcare in England, in response to the Cumberlege review into treatments that caused avoidable harm. But it rejected calls to set up an independent redress agency for the people harmed or to appoint a taskforce to implement the recommendations of the review, which examined pelvic mesh, Primodos, and sodium valproate. The government was still considering whether doctors' financial and non-pecuniary interests should be declared, but Nadine Dorries, health minister, indicated that this would be implemented in the future.



MEDICINE

Research news

Fried food links to major heart and stroke risk

An analysis from studies involving more than 1.3 million people found that the highest category of weekly fried food consumption, when compared with the lowest, was associated with a 28% raised risk of major cardiovascular events, a 22% raised risk of coronary heart disease, and a 37% raised risk of heart failure. With each extra 114 g weekly serving these risks substantially increased by 3%, 2%, and 12%, respectively, researchers reported in the journal *Heart*.



Consumption of fried food was linked to raised risk to the heart

ago by Simon Wessely, former president of the Royal College of Psychiatrists. The Department of Health and Social Care has said changes needing legislation will be in a draft Mental Health Bill for consultation next year.

Parliament

Lords act to combat forced harvesting of organs

The House of Lords passed an amendment to the Medicines and Medical Devices Bill that aims to protect medical institutions and practitioners from becoming unwittingly complicit in Chinese state sanctioned forced organ harvesting. The amendment gives ministers the power to regulate against the use of human tissues, organs, and cells from overseas that may have been forcibly harvested. The bill is expected to become law in the spring.



Mental Health Act reform aims to tackle poor care

Major changes were announced to mental health laws in England and Wales that aim to ensure parity with physical health services, put patients' views at the centre of their care, and tackle racial inequalities. The proposals came in a government white paper, building on reforms recommended by a review of the 1983 Mental Health Act two years

UK "will miss targets" without urgent action

The government will miss key targets to improve healthy ageing unless it acts urgently, an inquiry concluded. The House of Lords Science and Technology Committee said ministers should produce a strategy for how to achieve five extra healthy years of life by 2035, reporting progress annually, and should set out a clear plan for reducing health inequalities over the next parliament. Messages on healthy living weren't effective, and more targeted advice and interventions were needed, said the report.

Maternity care

Bedford Hospital must improve urgently—CQC

Bedford Hospital's maternity services were served with an urgent warning notice after an unannounced inspection, sparked by 14 complaints from August to November 2020. The CQC placed conditions on the registration of Bedfordshire Hospitals Trust after finding the service did not always have enough staff with the right qualifications and experience to keep women safe from avoidable harm.

Cite this as: *BMJ* 2021;372:n154

VACCINES

A survey of 11 700 British adults found that vaccine hesitancy was highest among black people, with 72% saying they were unlikely or very unlikely to be vaccinated, followed by Pakistani and Bangladeshi groups (42%).

Among white British and Irish the likely refusal rate

was 16%

[UK Household Longitudinal Study]

SIXTY SECONDS ON... COVID INFLUENCERS



PARDON?

Get with the programme, Grandad. Influencers are very... influential these days. And they don't just encourage people on social media to buy things they don't need.

REALLY? WHAT ELSE DO THEY DO?

Help spearhead public health campaigns, it seems. The fact checking organisation Full Fact did some digging and found that the government paid £63 000 to 42 social media influencers to promote the national NHS test and trace service last year. This equates to roughly £1500 per influencer on average.

TOUGH GIG

Indeed. Not only were they trying to promote a troublesome brand (sorry, Dido) but influencing people isn't as easy it sounds. Only a select few people with very large social media followings—such as *Love Island* contestants Shaughna Phillips (below) and Josh Denzel, and professional hockey player Henry Weir—were deemed fit for this task.

THIS SOUNDS MORE CARROT THAN (HOCKEY) STICK?

You could say that. As part of a coordinated advertising campaign last year, the government paid the celebrities to share messages of support for the NHS and the test and trace system on their social media pages.

THAT'S ONE WAY TO WIN FRIENDS. WHAT WAS THE RATIONALE?

The Cabinet Office told Full Fact that as part of its wider communications strategy for raising awareness of the service and the importance of testing for covid-19, it decided to work with "key micro and macro influencers to reach young adults in a channel they regularly engage with," alongside more traditional methods of marketing.



I FEEL OLD. IS THIS TREND HERE TO STAY?

Quite possibly. With vaccinations, diagnostic services, and health checks to promote, don't be surprised if we see influenza influencers and YouTestTubers professing their love for the NHS before long.

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2021;372:n151

Frail patient alert after Norway vaccine deaths

What we need to know is how the observed death rate... compares with the expected death rate

Azeem Majeed

Doctors in Norway have been advised to assess severely frail and terminally ill patients to determine whether the benefits of vaccination outweigh the risks of possible side effects, after reports indicated that vaccine side effects may have led to deterioration and death of some patients.

Reports of 33 suspected adverse drug reactions with fatal outcomes after administration of the Pfizer and BioNTech vaccine had been received by the Norwegian Medicines Agency as at 17 January. All the people who died were over 75. Around 42 000 people are believed to have received the first dose of the vaccine so far in Norway.

The agency has investigated 13 of the deaths so far and concluded that common adverse reactions of mRNA vaccines, such as fever, nausea, and diarrhoea, may have contributed to the deaths of some frail patients.

Although for most elderly frail people any vaccine side effects will be outweighed by a reduced risk of a severe covid-19 disease, for those with the severest frailty even relatively mild side effects can have serious consequences, the Norwegian Institute of Public Health said. And the benefits of the vaccine to those with a very short life expectancy may be marginal or irrelevant, it said. The institute is now recommending that doctors consider the benefits and disadvantages of giving the vaccine to extremely frail patients (such as those whose frailty is ranked 8 or 9 on the Clinical Frailty Scale or equivalent) and terminally ill patients ahead of vaccination.

Azeem Majeed, professor of primary care and public health at Imperial College London, said, "The experience of Norway shows the importance of monitoring the safety and efficacy of the new covid-19 vaccine. They are now being given to millions of people globally, including many people who will be older and frailer than the participants in the clinical trial."

"Evidence based information"

Majeed added, "Some older people would be expected to die, and what we need to know is how the observed death rate in older vaccine participants compares with the expected death rate. Without this information, it's difficult to draw any conclusions and give older people evidence based information on the safety of the vaccines."

The UK was the first country to roll out the Pfizer-BioNTech vaccine, but the Medicines and Healthcare Products

MEDICAL agency reports all the **33** people who died were over 75

Maternal deaths gap because of ethnicity is "unacceptable"

Urgent action is needed to tackle systemic biases contributing to unequal mortality outcomes in ethnic minority women and women facing multiple problems and deprivation, say experts.

The authors of an analysis of maternal deaths in the UK, issued by Oxford University's Nuffield Department of Population Health, say the pandemic is likely to have worsened the disparities.

Four times as likely to die

Black women are four times as likely as white women to die in pregnancy or childbirth, says the seventh annual report from MBRRACE-UK (Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries). Asian women face a twofold risk, and women in the most deprived areas are almost three times as likely to die as those in the most affluent areas.

The report used surveillance data from 2016-18 on women



who died while pregnant or up to a year later. The proportion known to have been experiencing multiple disadvantages when they died rose to 8%, from 6% in the 2019 report. Such women often face mental ill health or domestic abuse and may misuse substances.

Maggie Rae, president of the Faculty of Public Health, said, "Women who live in more deprived areas continue to be at greater risk of dying during or after pregnancy, and many of the complex factors underlying this increased risk need action much more widely than in maternity services, beyond the health sector, and often long before

pregnancy. We need to address this to reduce deaths of women as well as their babies."

The report said that pregnancy remained "very safe" in the UK. In 2016-18, of 2.2 million women who gave birth, 547 died during pregnancy or up to a year afterwards from causes associated with their pregnancy. In that period 34 black women, 15 Asian women, and eight white women died among every 100 000 giving birth.

The report said that these figures were "fundamentally unchanged" from the 2019 report and that, despite encouraging responses from the NHS and government agencies, sustained focus was needed.

Marian Knight, lead author for MBRRACE-UK and professor of maternal and child population health at Oxford University, said that disparity in maternal mortality because of a woman's ethnicity was "unacceptable."

She added, "It is equally unacceptable for women with pre-existing medical conditions such as epilepsy to receive a lower standard of care."

Death in epilepsy

The analysis reported a "concerning rise"—almost doubled from the previous three years—in maternal mortality from sudden unexpected death in epilepsy. In many instances these deaths were linked to inadequate medicine management before or during the woman's pregnancy.

Knight said, "Systemic biases prevent women with complex and multiple problems receiving the care they need. This needs to be addressed urgently, particularly since the impacts of social and ethnic inequalities, multiple disadvantages, and epilepsy are likely to have been amplified during the pandemic."

Matthew Limb, London

Cite this as: *BMJ* 2021;372:n152



As soon as WHO has gained a full understanding of these events, the findings and any changes to recommendations will be immediately communicated

World Health Organization

Regulatory Agency has yet to publish any data on adverse reactions to it.

The World Health Organization said it had been in touch with the Norwegian authorities and the European Medicines Agency to get more information. "As soon as WHO and partners have gained a full understanding of these events, the findings and any changes to current recommendations will be immediately communicated to the public," it said.

In a statement Pfizer UK said, "We are working with the Norwegian Medicines Agency (NOMA) to

gather all the relevant information. Norwegian authorities have prioritised the immunisation of residents in nursing homes, most of whom are very elderly with underlying medical conditions and some who are terminally ill.

"NOMA confirm the number of reports so far is not alarming and in line with expectations. All reported deaths will be thoroughly evaluated by NOMA to determine if these reports are related to the vaccine."

Ingrid Torjesen, London
Cite this as: *BMJ* 2021;372:n167

Assess effects of extending Pfizer vaccine dosing interval, expert urges

A leading statistician has written to England's health secretary, Matt Hancock, urging him to investigate the effects of extending the gap between the first and second dose of the Pfizer BioNTech vaccine.

Sheila Bird, former programme leader at the MRC Biostatistics Unit at Cambridge University and a member of the Royal Statistical Society's covid-19 taskforce, said that, while deviating from the recommended dosing interval of three weeks could be the right decision that saves more lives, ministers should be sure of the consequences.

In a 30 December letter, NHS England told healthcare staff to prioritise giving the first doses of vaccine (either Pfizer-BioNTech or Oxford-AstraZeneca) to as many people as possible on the priority list. Second doses should then be given up to 12 weeks after the first.

Unlike the Oxford vaccine trials, however, the Pfizer trial did not test

different dosing intervals, with all participants receiving their second dose 21 days after the first. Results published in the *New England Journal of Medicine* reported that efficacy between the first and second doses was 52%, though Pfizer has said that there is no evidence of efficacy for the first dose after the 21 days.

"Precise pattern"

In her letter, Bird said, "As noted by the British Society for Immunology, we do not know the precise pattern for how effectiveness for Pfizer BioNTech's mRNA vaccine wanes after the first dose if the second is not administered as in Pfizer's trial."

She said the UK's rapid rollout of the Pfizer vaccine meant that 800 000 people could be randomised in just two weeks, enabling researchers to ascertain outcomes such as covid diagnoses and related hospitalisations.

Elisabeth Mahase, *The BMJ*
Cite this as: *BMJ* 2021;372:n162

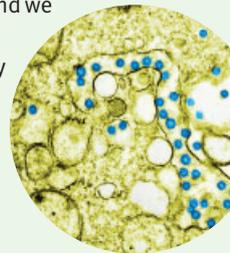
"Past infection protects but may not stop spread"

People previously infected with SARS-CoV-2 are likely to be protected against reinfection for several months but could still carry the virus in their nose and throat and transmit it to others, finds a study that regularly tested thousands of healthcare workers.

The preprint reported interim results from Public Health England's Siren study between 18 June and 24 November. In that period the researchers detected 44 potential and 409 new infections, equating to an 83% rate of protection from reinfection, which seemed to last for at least five months from first becoming sick.

But the research team warned that early evidence from the next stage of the study indicated that some people who were themselves protected by antibodies still carried high numbers of the virus and could infect others.

Susan Hopkins, PHE's senior medical adviser and Siren lead, said, "We now know that most of those who have had the virus, and developed antibodies, are protected from reinfection, but this is not total and we do not yet know how long protection lasts. Crucially, we believe people may still be able to pass the virus on."



PCR and antibody testing

NHS staff who volunteered for the study were assigned to either the positive cohort (antibody positive or prior PCR antibody test positive) or negative cohort (antibody negative, not previously known to be PCR antibody positive). They attended PCR and antibody testing every two to four weeks and completed fortnightly questionnaires on symptoms and exposures.

In the study period 20 787 staff were included in the analysis, of whom 6614 (32%) were assigned to the positive cohort and 14 173 (68%) to the negative. By 24 November 409 new infections were detected in the negative cohort, of whom 249 (79%) were symptomatic.

The researchers detected 44 potential reinfections in the positive cohort, 15 (34%) of which were symptomatic. Some 42 were defined as possible, and two were defined as probable. This compared with 318 new PCR positive infections (249 symptomatic) and 94 antibody seroconversions in the negative cohort.

The study team said that the results gave no insight into the effects of vaccines or the more transmissible variant, but these factors will be considered in future analysis.

Elisabeth Mahase, *The BMJ*
Cite this as: *BMJ* 2021;372:n124



20 787 staff (84% female, 88% white, median age 45.9) were included in the analysis, of whom 6614 (32%) were assigned to the positive cohort and 14 173 (68%) to the negative cohort. By 24 November 409 new infections were detected in the negative cohort

When to start invasive ventilation is the “million dollar question” in covid care

Options for ventilating covid-19 patients have expanded since the first wave of the pandemic, but doctors are unsure of the best management pathway, because evidence is lacking. **Ingrid Torjesen** reports

During the first wave of the covid-19 pandemic almost three quarters of patients who were admitted to critical care received invasive ventilation, and one in two received it within 24 hours of admission. Now the numbers are around half that. Most receive non-invasive respiratory support instead, such as high flow nasal oxygen or continuous positive airway pressure (CPAP) by machine.

The pace of the move away from invasive ventilation varies among hospitals and has been driven by greater clinical experience of treating covid patients, by data associating invasive ventilation with higher mortality, and by the ventilation options available.

When to move patients from facemask CPAP to a ventilator “is really the million dollar question,” said an intensive care consultant from Surrey, who asked to remain anonymous. “We’ve had people who have had CPAP for weeks, maybe even a month, but they prefer to carry on with it than go on a ventilator. We haven’t really had good data to tell us what the right thing to do is. I hope that’s coming through quickly, because then I would be more confident in my approach.”

Annemarie Docherty, honorary consultant in critical care and researcher at the University of Edinburgh, agreed. “We’ve all adopted CPAP and non-invasive ventilation on no evidence, maybe an anecdote, which is the first time that we’ve ever done anything sort of on Twitter, and it’s not innocuous,” she said.

“We’re seeing lots of patients with injuries to their lungs just from the non-invasive mask—so there’s definitely a group of patients to whom we are doing harm, and we should

TRENDS IN CRITICAL CARE IN ENGLAND, WALES, AND NORTHERN IRELAND

| | Second wave (patients admitted 1 Sep to 31 Dec 2020) | First wave (patients admitted to 31 Aug 2020) |
|-----------------------------------------------------------------------------|------------------------------------------------------------|-----------------------------------------------------|
| Total covid hospital admissions* | 142553 | 129459 |
| Covid patients admitted to critical care | 10149 (7.1%) | 10935 (8.4%) |
| Discharged | 4927 (48.5%) | 6623 (60.6%) |
| Died | 2994 (29.5%) | 4311 (39.4%) |
| Still receiving care | 2228 (22.0%) | 1 (0.0%) |
| Percentage of patients receiving invasive ventilation within first 24 hours | 24.9% (2216/9563)** | 54.3% (5866/10935) |
| Advanced respiratory support at any point | 3427 (43.7%) | 7878 (72.1%) |
| Basic respiratory support only | 4073 (51.9%) | 2790 (25.5%) |
| No respiratory support | 343 (4.4%) | 264 (2.4%) |
| Mean age of critical care patients (years) | 60.4 | 58.8 |
| Mean length of hospital stay before intensive care admission (days) | 3.0 | 2.5 |
| Patients requiring renal support | 1107 (14.1%) | 2926 (26.8%) |
| Duration of critical care among survivors (median days) | 6 | 12 |
| Duration of critical care among non-survivors (median days) | 10 | 9 |

Advanced respiratory support: invasive ventilation, bilevel positive airway pressure (BPAP) by trans-laryngeal tube or tracheostomy, continuous positive airway pressure (CPAP) by trans-laryngeal tube, extracorporeal respiratory support.

Basic respiratory support: >50% oxygen by facemask, close observation because of potential for acute deterioration, physiotherapy and suction to clear secretions at least two hourly, recently extubated after a period of mechanical ventilation, mask or hood CPAP/BPAP, non-invasive ventilation, CPAP by tracheostomy, intubated to protect airway.

Adapted from Intensive Care National Audit and Research Centre report on covid-19 in critical care: England, Wales, and Northern Ireland, 31 December 2020.

*Total number of patients from <https://coronavirus.data.gov.uk/details/healthcare>.

**Data not available for all patients.

be moving earlier towards intubating them, I think.”

Mervyn Singer, professor of intensive care medicine at University College London, said, “The argument is that if you persist for a long time, just the heavy breathing might cause lung damage of its own. There are one or two hospitals that still adamantly say that you need to invasively ventilate everybody and that you shouldn’t be non-invasively ventilating.”

Trial under way

No good evidence exists from clinical trials on the use of non-invasive respiratory support such as high flow nasal oxygen outside critical care settings, said Manu Shankar-Hari, a

We haven’t had good data to tell us what the right thing to do is. I hope that’s coming through quickly, because then I would be more confident in my approach
Surrey consultant

consultant in intensive care medicine at King’s College London. “The RECOVERY-RS trial will address that partly,” he said. This trial compares high flow nasal oxygen and CPAP with standard care (normal oxygen through a mask or nasal cannula), and patients will be given invasive ventilation if clinically required.

But Singer said, “The question I would have loved RECOVERY-RS to ask is when the right time is to start invasive ventilation, because in our practice we start relatively late because of resource limitations.”

The danger in providing such non-invasive forms of respiratory support on a medical ward is that, eventually, when patients don’t respond or



We're seeing lots of patients with injuries to their lungs from the non-invasive mask—so there are patients to whom we are doing harm Annemarie Docherty



There are hospitals that still say you need to invasively ventilate everybody and you shouldn't be non-invasively ventilating Mervyn Singer



The danger of non-invasive support on a medical ward is that when patients require more invasive support they are much more unwell Manu Shankar-Hari

they deteriorate and require a more invasive form of respiratory support, they are much more unwell, said Shankar-Hari. And he pointed out that it's often younger patients who initially receive respiratory support on medical wards, because they're more able to cope with the symptoms when admitted to hospital, at least initially.

If the strain on hospitals continues to increase it will be these patients on medical wards who are at particular risk, Docherty warned. "Probably the biggest [additional] mortality will come among patients who can't get into intensive care because they are not flagged as deteriorating, because there's not enough people to review them," she said. "When patients are intubated, they're a bit more stable."

Renal support

The reduction in the proportion of patients receiving invasive ventilation has been accompanied by a fall in the proportion requiring renal support. This may be because invasive ventilation can affect the kidneys in a number of ways, said Singer.

Patients with covid-19 require heavy sedation for invasive ventilation, and these drugs often cause a dramatic drop in blood pressure. Vasopressor catecholamines, such as norepinephrine, are then given to elevate the blood pressure and can have an adverse impact on the kidneys by affecting intrarenal perfusion.

Furthermore, said Singer, "When you put somebody on a ventilator

you're giving positive pressure ventilation, which also has a negative effect on the kidney through an increase in renal venous pressure and congestion. There is also a tendency to keep patients on ventilators quite dry to 'protect the lungs,' and that too can compromise renal perfusion."

Oxygen supplies

High flow respiratory support such as CPAP also requires more oxygen than invasive ventilation or a facemask, and supplying oxygen for patients with covid-19 is causing problems for some hospitals. Already this year St Helier Hospital in Sutton, south London, has had to transfer some patients to other hospitals because its ageing infrastructure could not provide sufficient quantities.

A spokeswoman for Epsom and St Helier University Hospitals Trust said that a new vaporiser had now been installed at the hospital that would treble the supply of piped oxygen available to patients.

While more patients are in hospital now than in the first wave, in some ways working conditions are less stressful, as there is no longer a shortage of personal protective equipment, and doctors have some evidence and experience to inform their decisions, said the intensive care consultant from

Surrey seeking the million dollar answer. "In the first wave everyone was understandably panicked until we knew what the best thing to do was, so they were doing lots of unusual things, which made me very stressed," said the consultant. "I didn't like it. People were desperate, perhaps just keen to help, but they were doing odd things which were potentially harmful."

New variant

The recent large rise in the number of covid cases has been attributed to the greater transmissibility of a new variant of SARS-CoV-2 that was first identified spreading across London and the south east of England. So far no evidence has shown that this variant is more virulent or pathogenic or that it leads to a greater proportion of patients needing intensive care, and the Intensive Care National Audit and Research Centre hopes to be able to confirm this.

Its director, Kathy Rowan, said, "We may be able to look by region and time period, to see if there were any differences in patient characteristics and outcomes in London and the south east creeping in at the point where we felt the new variant became dominant."

Ingrid Torjesen, London

Cite this as: *BMJ* 2021;372:n121



NEEL HALU/PA

THE BIG PICTURE

Gothic sanctuary gives hope for the future

To the sound of organ music, hundreds of people aged over 80 receive their Pfizer-BioNTech covid-19 vaccination inside the grandeur of Salisbury Cathedral transept.

On Saturday 16 January the cathedral was turned into a pop-up vaccination hub by Sarum South Primary Care Network. Its co-clinical director Dan Henderson said around 1000 patients and staff were vaccinated in one day.

Nicholas Papadopoulos, the dean of Salisbury, told the *Guardian*, “This place has stood here for 800 years to give glory to God, and to serve the city and the region. What better way could there be to do that than hosting Salisbury’s stage in the vaccination programme. It is absolutely wonderful.”

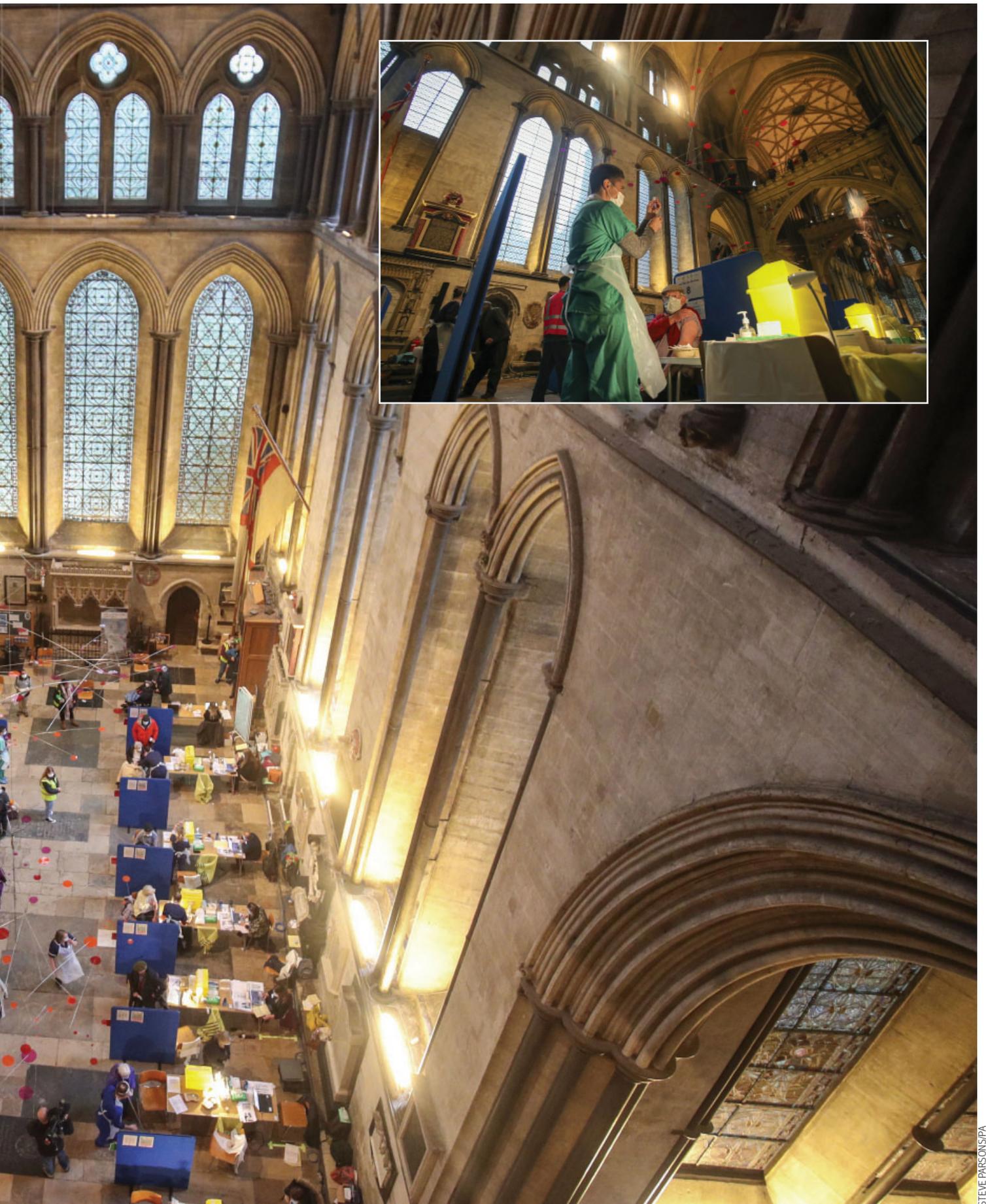
Lichfield and Blackburn cathedrals have also opened their doors to help the vaccination drive, along with race courses, sports halls, and other venues closed because of the current lockdown.

From the start of this week, across the UK people aged 70 and over and the clinically extremely vulnerable also began to be invited to join the 3.8 million people who have so far received their first vaccine dose. The government has pledged to offer a vaccine to everyone over the age 70, all health and social care workers, and clinically extremely vulnerable people by mid-February.

Alison Shepherd, *The BMJ*

Cite this as: *BMJ* 2021;372:n155





STEVE PARSONS/SPA

Covid-19 and moral distress in medicine

Simply working harder cannot resolve the conflicts caused by responsibility without autonomy

Doctors are accustomed to difficulty, to long hours, high stress, heavy responsibility. The job involves helping people navigate life's gravest challenges: death and dying, suffering, loss, and grief. For as long as there have been healers though, this has been part of the territory.

But as the profession draws deeply on its resources to respond to covid-19, a new concept is entering the mainstream: moral distress.^{1,2} And it is shining a light on the deepening structural afflictions of medicine in the UK, problems that predated covid and, unless they are resolved, will endure long beyond it.

Moral distress is a psychological harm arising when people are forced to make, or witness, decisions or actions that contradict their core moral values. While exposure to the suffering of others can lead to distress, it is not necessarily moral distress. But if serious and sustained resource constraints mean doctors cannot meet patients' needs, it can open the door to moral distress. If you know that delays to treatment will likely lead to serious harms, consider the effect of repeatedly being forced to place patients on ever lengthening waiting lists. Moral distress arises in the gap between what professional judgment dictates should be done and what healthcare systems permit. It is also associated with powerlessness—the impossibility of altering the situation so that professional acts can accord with professional values.

Guilt, shame, anger

The term entered health through nursing ethics⁴ and found traction among health professionals working in humanitarian crises, where professional norms have at times been profoundly challenged. Typical emotional responses to moral distress include feelings of guilt, shame, anger, and, in extreme form, disgust.⁵



VICTORIA JONES/PA

Situations strongly linked to moral distress include the rationing or triaging of scarce resources such as ventilatory support

If moral distress is sustained it can lead to moral injury—a deeper or more enduring harm that can lead to burnout and psychological trauma.

The term moral distress is increasingly used to describe the cumulative unease experienced by doctors struggling to fulfil their primary professional obligations in once highly resourced medical settings.

During the covid pandemic, situations strongly linked to moral distress include the rationing or triaging of scarce resources such as ventilatory support, intensive care beds, or protective equipment; de-prioritising patients who have substantial non-covid related health needs and who are likely to be harmed by treatment delays; being barred from work by covid rules when colleagues and patients desperately need help; making harrowing ethical choices without appropriate support; and denying patients access to vital social and emotional support because of infection control requirements. The list goes on.

It will be said that covid is exceptional. That every health system in the world is struggling. That there will be a reset. But covid is exacerbating existing pressures rather than creating new ones.

The slow tightening of the garotte of underfunding has created ideal conditions for moral distress, sapping the joy from the doctor-patient relationship, depleting the rewards of clinical medicine, swapping pleasure for grinding distress. Plenty of anecdotal evidence suggests it contributes to early retirement and to a general crisis of retention in medicine more broadly.

Ethical conflict

The NHS needs to be properly resourced. We must not allow permanent underfunding to place health professionals in unending ethical conflict. In the meantime, doctors must learn to recognise their own moral distress, identify its sources, and understand that they are not at fault. Open discussion and peer support are essential, acknowledging that simply working harder cannot resolve the conflicts born from responsibility without autonomy. Schwartz rounds⁶ can play a vital role here, but only if doctors have time to attend. Doctors must also be supported when making challenging ethical decisions, including ensuring access to ethical and legal expertise. Doctors must be psychologically—and contractually—permitted to make time for reflection and self-care. They cannot run on fumes indefinitely.

Revolutions are said to eat their children. Tragically, the same is true of dysfunctional organisations. They force virtuous employees into intolerable positions as professional codes collide with institutional diktat often rooted in resource constraints. Covid has highlighted how essential the NHS is to our collective wellbeing. It is beyond time to fund it effectively. Until then, all health professionals need support in managing moral distress—before its effects become too toxic.

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Vaccinating people who report allergies

Most patients can be reassured and vaccinated

Use of the Pfizer-BioNTech covid-19 vaccine in people with a history of severe allergies was temporarily stopped in the UK after two healthcare workers experienced anaphylactic reactions in early December. The Medicines and Healthcare Products Regulatory Agency (MHRA) stated that “any person with a history of anaphylaxis to a vaccine, medicine, or food should not receive the Pfizer/BioNTech vaccine.”¹

However, MHRA revised its position on 30 December after careful consideration based on enhanced surveillance of over one million doses of the vaccine in the UK and North America—including in jurisdictions where people with serious allergies were never barred from receiving the vaccine.² It found no evidence of an increased risk of anaphylaxis to the Pfizer-BioNTech vaccine among people with serious but unrelated allergy histories and advised that only people who had an allergic reaction to the first dose of this vaccine, or who previously had reactions to any of its components, should not receive it.

Risks to UK rollout

This is welcome news for people with severe allergies, but risks to the UK rollout of covid-19 vaccines remain because of the widespread dissemination of the allergy contraindication in the media.

The reporting of allergy as synonymous with anaphylaxis is concerning, since in the UK and US 20-40% of the population has at least one allergic disease,⁶⁻⁹ an umbrella term for multiple clinical syndromes (allergic rhinitis, anaphylaxis, allergic asthma, conjunctivitis, eczema and contact dermatitis, food allergy, and urticaria) caused by food, aeroallergens (including pollen),



TESSON/WANDZ/ABACA/PA

and immunologically mediated adverse effects of medicines.⁶

Before the Pfizer-BioNTech vaccine contraindication was announced, surveys reported that the public's willingness to be vaccinated with one of the covid vaccines ranged from 67% to 90%.¹⁰ That estimate has been fluctuating, however. In one study conducted from April to May 2020, 90% of parents and guardians of young children said they would accept a vaccine,¹¹ while in June, a similar questionnaire reported potential uptake to be roughly 70%.¹² By July, another UK study found that 64% of participants were “very likely” to accept a vaccine, with 27% unsure.¹³ Vaccine hesitancy seems to be highest in ethnic minority populations.¹⁰

Given that allergies are commonly reported, and public acceptance for a covid-19 vaccine seems to be waning, uptake of the Pfizer-BioNTech vaccine may be lower than hoped. Healthcare workers may also be reluctant to vaccinate people with any history of allergies. It is therefore essential that those planning and administering covid-19 vaccine programmes understand the evidence.

Importantly, history of severe allergy does not preclude vaccination unless that allergy is to the vaccine

History of severe allergy does not preclude vaccination unless that allergy is to the vaccine or its components

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or its components. Only one of the excipients in the Pfizer-BioNTech vaccine is a known potential allergen, polyethylene glycol (PEG 2000), and this is an inactive ingredient in more than 1000 medications. The Oxford-AstraZeneca vaccine does not contain PEG 2000 so remains an alternative for people with a history of allergy to this ingredient.² However, there is some cross-reactivity between PEG and polysorbate 80, an ingredient in the Oxford-AstraZeneca vaccine, so evaluation by an allergy specialist may be advisable before vaccination in anyone with a suspected PEG allergy history.¹⁴ Allergy is antigen specific, although people with one drug allergy may be more susceptible to other drug allergies than the general population.¹⁵

Lines of communication

The best approaches to vaccine hesitancy include “science, education, access, civil discourse, and debate,”¹⁶ not coercion or censorship. Vaccinators should be prepared to provide information, explain the difference between severe, moderate, and mild allergies, and clarify MHRA's decision making. People's views about covid vaccines may transfer to other vaccines, so maintain open lines of communication, and if vaccination is declined, then reassure people that they can return.

It may still be possible to safely vaccinate people with allergies to vaccine components.¹⁷ Allergists can assess patients who report allergy to a vaccine, injectable medication, or PEG and triage them into those able to be vaccinated with the routine 15 minutes of observation, those requiring 30 minutes of observation, and those who require skin testing to PEG and polysorbate before vaccination. Our hospitals have already launched such services and evaluation is ongoing.

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CHIP SOMODEVILLA/GETTY IMAGES

US HEALTH

How Joe Biden plans to heal healthcare in America

The world's highest number of covid deaths, a broken system, and a mess of unhelpful regulations imposed by his predecessor—**Joanne Silberner** examines what the new president can do to meet the challenges ahead

During his presidential campaign the Democratic candidate Joe Biden laid out some clear goals: expand access to health insurance, simplify the notoriously complex healthcare system, cut the costs of prescription drugs, and expand access to abortion. Then covid cast a shadow on the whole race for the White House.

As Biden prepared to take the oath of office on 20 January he faced the immediate challenge of dealing with the pandemic buffeting the US and reversing years of undercooked protection and prevention measures.

But he does have one thing on his side that he might not have expected at the beginning of the campaign: control of the US Senate, which the Democrats won in a closely fought 5 January run-off election in Georgia. With his party now in control of the White House, Senate, and House of Representatives, Biden has a good chance of getting at least some of his agenda approved.

Still, the Democratic majorities in the House and Senate are slim, and

some Democrats lean towards the conservative side, and some types of legislation require a “supermajority.” Health experts are divided on the fate of two of the president’s more ambitious plans: allowing an insurance plan run by government to compete against private insurers in the Affordable Care Act (also known as Obamacare, introduced under Barack Obama who Biden served as vice president) and lowering the age of eligibility for Medicare, the government insurance programme for people aged at least 65.

But the Senate majority does give Biden free rein to pick his own people for top posts without having to compromise with the Republicans. He may be able to open up and make some changes to Obamacare that will nullify a pending Supreme Court decision that could otherwise threaten its viability.

There are also several dozen more health related policy changes that Biden has the power to make without Senate approval. But first he has to confront covid-19.

The Trump administration has left “bird droppings” that must be dealt with to have a clean slate

Chris Jennings, Biden adviser

Pandemic action

Biden has been regularly briefed on the pandemic by respected scientists, including Anthony Fauci, head of the National Institute of Allergy and Infectious Diseases, who had been sidelined by Donald Trump’s administration. Biden has set up a scientific advisory board, and reportedly he demands regular updates from his staff on how vaccination planning is going, although staffers have complained that Trump’s officials have been slow to provide data.

Biden will ask all Americans to wear masks for his first 100 days in office, a major change from Trump, who rarely wore one and refused to endorse the practice. But the president has limited authority over mask wearing. It is the states that bear most of the responsibility for public health measures, and mask mandates vary across the country. Biden has said he’ll urge local and state governments to enact their own mandates and will require mask wearing on federal property and on interstate transport.

With vaccines, his administration is grappling with an uneven rollout that the Trump administration had basically left up to individual states, which are getting free vaccines but little funding for distribution.

Biden has promised 100 million vaccinations in his first 100 days. *Politico* reports that the president has serious concerns about delivering on this, given the lack of structure and resources officials encountered in the transition period. He has also said he’ll push to get first doses administered as soon as they can be made and distributed, rather than holding back stocks for second doses.

Five days before his inauguration, Biden warned Americans that things would get worse before getting better. He said he’ll be asking Congress for another \$20bn to speed up federal vaccination efforts, and is looking to extend insurance subsidies to more of the middle class.

Abortion rights

Three days after his inauguration in 2017 Trump announced the revival of the “Mexico City plan,” sometimes

known as the global gag rule. In its usual form this plan blocks family planning clinics anywhere from receiving federal family planning funding if they provide abortion or abortion counselling.

Trump's announcement continued a game of see saw that has lasted more than 30 years. First implemented by Ronald Reagan in 1984, Democratic presidents cancel it the first chance they get. Republican incumbents reinstate it. Trump's version—the harshest yet—banned not just family planning funding to any clinic that even mentioned abortion to its patients but also funds earmarked for treating HIV, malaria, and other infectious diseases. The policy quickly led to reduced access to family planning services in low income countries. Biden has promised to cancel it early in his presidency.

He has also promised to strengthen the Affordable Care Act, Obama's expansion of health insurance, which Trump vowed to repeal and replace. Throughout his presidency Trump repeatedly promised a new and better plan but never introduced one. He was, however, able to weaken Obamacare in several ways, including cutting funding for public information about the insurance programmes, allowing people to buy insurance that didn't offer all the benefits covered by the act, and allowing insurance policies that did not cover pre-existing conditions.

Back on the world stage

The Trump presidency had seen the US step back from global health leadership like never before, epitomised by last July's announcement that he was pulling the US out of the World Health Organization.

But the withdrawal process takes a year, and Biden promised to cancel the pullout on his first day in office. He will also put back in place a job eliminated by Trump, a high level appointment for global health security and biodefence.

Chris Jennings, a long time health adviser to Democratic administrations, told Kaiser Health News that the Trump administration has left "bird droppings" that must

be dealt with to have a clean slate. One of the most worrisome for the scientific community is a rule that prohibits the Environmental Protection Agency from considering the results of studies on pollution and other environmental issues unless the raw data are available. And since most of the relevant research relies on confidential patient information, the need for privacy and anonymity would mean many of the most conclusive studies would be off limits.

Another recently finalised rule requires the agency to ignore the economic costs of illnesses and deaths when totting up the total costs of air pollution. Which brings us to climate change. Citing his "America First" policy, Trump started the process of withdrawing the US from the Paris Agreement early in his presidency. The withdrawal was finalised on 4 November, the day after voting for the presidential election closed. Biden has promised to rejoin on the first day of his presidency.

Fixing the healthcare "system"

The Department of Health and Human Services (HHS) runs the Food and Drug Administration, the Centers for Disease Control, various government health insurance programmes, drug treatment agencies, and more. During his tenure Trump often second guessed or ignored advice from the agencies, and morale throughout HHS is low.

Don Berwick, a senior fellow at the Institute for Healthcare Improvement and former acting head of Medicare and Medicaid (the healthcare programme for people on low incomes or with disabilities), thinks the way to get things moving again is to start with morale. "From what I'm hearing, there's a level of demoralisation among people who've spent their careers trying to make good federal programmes that is profound," he says.

HHS will need to create new programmes, bolster old ones, and reverse some Trump changes, says Berwick, who was also an adviser to the Biden presidential campaign.



Joe Biden receives his second covid vaccination on 11 January

Biden has promised 100 million covid vaccinations in his first 100 days

He expects to see a renewed drive to fight the opioid epidemic, which has been overlooked during the pandemic.

On 8 January the Trump administration permitted the state of Tennessee to fundamentally change the financing for Medicaid. The new programme gives the state more power over how federal funds are spent, while putting a cap on total funding, regardless of need. Such an approach could destroy the programme. The *New York Times* reported that the current head of Medicaid has been pressing states to sign contracts that would make it difficult for them to alter any special deals they've made with the Trump government, which could make the Tennessee plan difficult to cancel.

One of Trump's rare bipartisan actions, taken just before the end of his presidency, was to sign legislation that eliminates "surprise billing," as of 2022. This is where a patient goes to a hospital that is part of their insurance plan but where the individual anaesthetist or the surgeon, say, may not be covered by that plan. Patients in the US regularly wake up from surgery to bills of thousands or tens of thousands of dollars for care that would have entailed only a small copayment had the doctor been in the plan.

Now Biden's people get to write the rules for one of the few health laws to come out of the Trump years that benefits patients.

Joanne Silberner, US coronavirus news editor, *The BMJ*

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Andrew Pollard: How the Oxford-AstraZeneca covid-19 vaccine was made

The leader of the clinical trials in the UK, Brazil, and South Africa tells **Elisabeth Mahase** how the vaccine came to be, how dosing was worked out, and whether it will stand up to the new variants



I realised that our lives were going to change completely. Straight away I was thinking that we needed a vaccine

Andrew Pollard was in a French taxi when he realised what was coming. On his way to a meeting to present his group's research on typhoid, he happened to share a ride to the airport with John Edmunds of the UK Scientific Advisory Group for Emergencies, and they discussed a new virus emerging in China.

"He had a fairly catastrophic view of what was likely to happen to the world from that point," says Pollard. "That was an incredibly chilling moment because I realised that our lives were going to change completely during 2020. Straight away I was thinking that we needed a vaccine."

A multi-award winner, Pollard has become one of the faces of the world's pandemic vaccine effort. As chair of the UK's Joint Committee on Vaccination and Immunisation and the European Medicines Agency's scientific advisory group on vaccines, he knew better than anyone the size of the task ahead. But, as an experienced climber (he was deputy leader of the successful 1994 British Mount Everest Medical Expedition), he knows that mountains are there to be conquered.

In light of the emerging new variants, how much would the virus need to mutate to make a vaccine ineffective?

The vaccines that are currently in late stage development, or that are authorised for use, use a large part of the spike protein, which is a very big protein. So, the immune response is against lots of different bits of that protein. This means that, to completely escape, the virus has to mutate quite a lot—so this may give some advantages against escape happening in the short term.

Mutants can arise that escape from the vaccine when there's a lot of pressure on the virus to change. At this moment hardly anyone in the world has been vaccinated and hardly anyone in the world has had disease, even though it feels like a huge impact. Most people have not had an infection yet. And so, the virus is not under huge immune selection.

When lots of people have had disease or been vaccinated, the virus is going to come under a lot of pressure, and when that happens some viruses just can't compete against that immunity.

Will it mutate instead? With this coronavirus we don't know the answer to that question yet, and

that's why surveillance is going to be critical in the year ahead to make sure that we're not in a position where, at the point of population immunity, the virus escapes. And if it does, we need to know that, so that we can redesign the vaccines.

How easy would it be to redesign a vaccine to counter mutations?

For the RNA vaccines and the viral vectors it's relatively straightforward, because you just have to synthesise a new bit of DNA in our case—or RNA in [the Pfizer and Moderna] cases—and then insert that into the new vaccine. Then there's a bit of work to do to manufacture the new vaccine, which is a reasonably heavy lift. But the same processes would be used.

And there will almost certainly need to be some testing, whether it's in animals or humans, to show you can still generate immune responses, and then the regulator would have to approve that new product.

SARS-CoV-2 is new to us, but it's from a known family of viruses. Was this helpful in getting the vaccine effort off the ground?

This has been the great thing about this being a coronavirus, because we

WHAT HAS IT BEEN LIKE TO HAVE BEEN IN THE INTERNATIONAL SPOTLIGHT?

To be honest, the year has been in many ways not exceptional . . . we've been doing the mundane stuff we normally do—it's the day job. And yet you step into the outside world, and suddenly you realise that everyone's watching you and wants to know exactly what you're going to do next and why you did what you did yesterday. I think in many ways it's been a completely normal year in vaccine development. What's been different about it has been much longer hours and then immense pressure on the team, because of that external spotlight on us and the urgency of a pandemic.





STEVE PARSONS/PA

The Duke of Cambridge meets Pollard last June during a visit to the Oxford Vaccine Group's facility at the Churchill Hospital in Oxford

know so much about the biology of these viruses and particularly how to make vaccines against them.

Over the past 20 years we've had two huge outbreaks of coronaviruses: one back in 2002, which was the SARS coronavirus with about an 11% mortality, and then about eight years ago the MERS coronavirus, which had a 35% mortality. Because those were so horrific and there were around a thousand cases on each occasion, lots of efforts went into making vaccines, which were mostly tested in animals.

We found out from those studies that making immune responses against spike protein could result in protection. My colleague Sarah Gilbert was already working on a MERS coronavirus vaccine just before the [current] pandemic. It was essentially switching the spike protein from the MERS coronavirus to the spike protein of SARS-CoV-2.

All the current vaccines are two dose regimens, and the dose interval has been intensely debated. Is there a case for a one dose strategy or two half doses?

The two dose strategy for our vaccine is actually a change. We originally

planned a one dose strategy, and that was really going back to those discussions with the modellers back in February, where it looked as if the UK would be struck by a huge first wave of disease that was devastating. My thinking then was that, if you waited for two doses, we'd have enormous numbers of inpatients and deaths—whereas, if you got one dose, we might be in a much better position to manage.

So, the original strategy when we set out in our trials was just a single dose. But we had a subgroup where we gave two doses, and we found in that group that we ended up with much better immune responses. We went back to the regulators and agreed that we'd move to a two dose strategy, with the idea that you hopefully get some protection from the first dose but that the second dose would give better and perhaps more sustained protection.

As a result, we had to then manufacture enough doses to give the second dose, and that inevitably led to a delay in having the second dose available. That's given us this really interesting phenomenon in our trial, which wasn't intended at the beginning, where we [now] have

Absolutely fascinatingly those who had a longer dose interval actually make much better immune responses after the second dose

some people who were vaccinated a month after the first dose and some people, because they'd been vaccinated before the manufacturing happened, who had to wait almost three months for their second dose.

So, we've got this spectrum of people between four and 12 weeks who were vaccinated, and the regulator has approved that interval because there's a lot of data. Absolutely fascinatingly, and perhaps predictably, those who had a longer interval actually make much better immune responses after the second dose. We see that with other vaccines, such as the cervical cancer vaccine.

The half dose has an advantage of dose sparing, but the vast majority of the data that we have is around two full doses. For the regulator, that's the compelling data package. The downside [to a half dose strategy] is that it's a bit more complicated to deliver for a practitioner who has to decide whether this is a half dose person or a full dose person.

Why does a longer dose interval seem to provide a better immune response?

It's almost certainly because the immune response matures after you

give a first dose, and, if you give it long enough to mature, you get a very good memory booster response to the second dose. If you have the second dose too early the immune response hasn't matured fully: there's a bit of negative feedback so it doesn't overshoot the mark, and you get a much smaller response to the second dose.

Are more data being collected on these dosing regimens?

The analysis that has led to the UK authorisation of the [Oxford-AstraZeneca] vaccine was an interim analysis, and so we still have 23 000 people being observed in my trials in the UK, Brazil, and South Africa. We're accumulating more data, and that may be very important because we'll have data on the new variant and hopefully efficacy against the new variants, both here and in South Africa.

We don't have any new trials planned to look at different regimens here in the UK, but we're moving on to new trials to evaluate different age groups—for example, children.

Why did your group wait longer than the other trials to release its phase III protocol?

All the way through I think we've followed the normal processes,



The Oxford /AstraZeneca vaccine was developed at the the Jenner Institute (above)



GREG BLATCHFORD/SHUTTERSTOCK

and actually, for our studies, we've got five publications on the clinical trials. All of the data are out there for people to see. And it's a bit perplexing that there's this constant accusation of a lack of transparency. It's actually something that, as a university, we're absolutely committed to and have been doing all the way through.

What we normally do with our research projects is write a protocol paper, and *BMJ Open* is one of the places we usually launch those. I have to say that, in this pandemic, we've just been a bit busy. We didn't focus on publishing a protocol paper as we've gone along; we just said that we'll put it in the publications when we get there. But I think it's

We still have 23 000 people being observed in my trials in the UK, Brazil, and South Africa

just the scale of what we've been doing as a small university research group: we just couldn't do everything that maybe the big pharmaceutical companies could.

What can the UK learn from the covid-19 vaccine development?

We could be better set up in the UK than we are, and we're one of the best countries in terms of being able to stand up multiple trial sites. In the UK we have 19 trial sites helping run the trials, and they were set up in about three weeks. They've done an amazing job in setting up, but they didn't have a dedicated infrastructure already in place. It required a lot of work to get that up and running.

There are multiple vaccine centres already established in the US, where they're doing vaccine development, vaccine research and evaluation, and laboratory work on testing immune responses. We have very little of that in the UK, so [one thing is] having more of this established, well funded, and running so that capacity is there on the research side.

And then there's the clinical delivery side. I think that one of the real stresses for everyone was being able to find the staff, to find the space and the training required to stand up a large scale study. If we were doing more of this day to day, I think we could do even more than we were able to do—and more quickly.

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Andrew Pollard has recused himself from the JCVI's meetings and discussions on covid-19 to prevent any conflict of interest

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Pollard receives his own covid-19 vaccine from Sam Foster at the Churchill Hospital in Oxford on 4 January

STEVE PARSONS/SPA