this week

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GETTYIMAGES

NHS model is not working, say leaders

The scale of the crisis facing the NHS has been laid bare in a leaked discussion among health service leaders in Scotland exploring radical changes to the way services are run.

A report of the discussion among the NHS chief executives, which was leaked to the BBC, included "designing in" what would in effect be a two tier health service, with wealthy people asked to pay for treatment. Other suggestions were to halt the use of new drugs unless they save the NHS money, embarking on "fundamental reform" of a primary care system that "no longer works today," increasing the "risk appetite" in hospitals to discharge patients after a maximum of 23 hours, and curtailing some free prescriptions.

Humza Yousaf, the Scottish health secretary, dismissed suggestions Scotland would move away from the principle of an NHS free at the point of need. He said on 21 November that services would continue to be based on patients' needs and would remain publicly owned and publicly operated. The UK's immigration minister, Robert Jenrick, delivered a similar message on TalkTV the same day: "We certainly don't have any intention to introduce charges to the NHS."

Yet the discussion illustrates the challenge to maintain a model of NHS care that dates back to 1948. The tone of the discussion in the leaked documents indicates that the most senior administrators in Scotland believe that things cannot continue as they are.

The minutes of the meeting refer to a "billion pound hole" in the Scottish budget and warn it is not possible to continue to run the current range of programmes while remaining safe and doing no harm. They add that "unscheduled care is going to fall over in the near term before planned care falls over." They conclude, "The fundamental model of healthcare is not working for us."

Iain Kennedy, chair of BMA Scotland, called for an honest, national conversation on how to make the NHS sustainable. "Clearly, as these papers show, parts of this discussion are already happening, behind closed doors.

"NHS boards have a nigh-on impossible task in making the budgets provided deliver everything being asked by the Scottish government. Things won't magically get better—we need an open and honest discussion, and we need change, urgently."

In a speech to the Confederation of British Industry the same afternoon Rishi Sunak said, "I grew up in an NHS family. It's in my blood, and as your prime minister I will always protect an NHS free at the point of delivery."

Bryan Christie, Edinburgh

Cite this as: *BMJ* 2022;379:o2813

Humza Yousaf, the Scottish health secretary, has denied that there is any plan to stop Scotland's NHS being free at the point of delivery

LATEST ONLINE

- Sexual health services are at "breaking point" after £1bn in cuts since 2015
- COP27: Countries agree "loss and damage" fund to help poor countries hit by climate disasters
- Founder of blood testing company that faked technology is sentenced to 11 years in prison

SEVEN DAYS IN

Doctors found not guilty of public disorder over Lambeth Bridge climate protest

HELENA SMITH

Six doctors and a nurse have been acquitted of breaching public order laws following a hearing at the City of London magistrates' court. GPs David McKelvey, Chris Newman, Mark Russell, and Patrick Hart, consultant obstetrician Alice Clack, clinical psychologist Rosie Jones, and specialist nurse Anna Bunten were found not guilty of breaching section 14 of the public order act after they blocked Lambeth Bridge on 10 April. They had joined the group Extinction Rebellion, displaying a banner saying "For health's sake, stop financing fossil fuels."

District judge David Robinson said, "I was impressed by the integrity and rationality of their beliefs" and "their evidence was highly moving."

Newman (pictured holding sign, left) said that although medical institutions had been publishing articles about the risks of climate change to health that alone was not enough. "Protest, like this one, is like attempting to shock a failing heart, in the hope it will change its rhythm. The *Lancet* said recently, 'There is some evidence that disruptive or radical non-violent actions . . . are successful at garnering public attention for a cause.' Thankfully, today the court recognised that right to protest," he said.

Zainab Hussain, *The BMJ* **Cite this as: *BMJ* 2022;379:o2783**

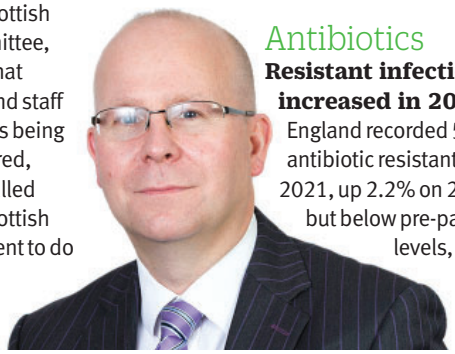
Workforce

Junior doctors head for industrial action ballot

A ballot for industrial action by junior doctors in England will open on 9 January, and the BMA says "all potential options [are] on the table." The move followed a vote by the association's Junior Doctors Committee last month, after the government failed to respond to its demands over pay and conditions. BMA representatives said they had "no choice but to take industrial action" at the failure to recognise their important contributions during the covid pandemic and the effects of soaring inflation.

Scotland's GP services reach breaking point

Eight in 10 general practices in Scotland that responded to a BMA survey said demand was exceeding their capacity, 42% substantially so. A third of practices reported at least one GP vacancy, up 6% since last year. Andrew Buist (right), chair of the BMA's Scottish GP Committee, warned that patient and staff safety was being endangered, and he called on the Scottish government to do more to recruit and retain GPs. "Doctors are leaving the profession because they are exhausted, burnt out, and cannot see the light at the end of the tunnel," he said.



Covid-19

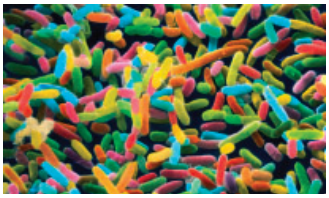
"Grotesque inequity" affects Paxlovid courses

Wealthy nations have secured almost three times as many courses as developing countries of Pfizer's covid oral antiviral drug Paxlovid (31.8 million *v* 11.2 million courses), found an analysis by Oxfam and the People's Vaccine Alliance. Paxlovid, a combination of nirmatrelvir and ritonavir, is strongly recommended by WHO for people with non-severe covid-19 who are at the highest risk of hospital admission. Catherine Kyobutungi, executive director of the African Population and Health Research Center, said, "Right now, [oral antivirals are] nearly exclusively accessible to people in the richest countries. It's grotesque inequality and it kills."

Antibiotics

Resistant infections increased in 2021

England recorded 53 985 severe antibiotic resistant infections in 2021, up 2.2% on 2020 (52 842) but below pre-pandemic levels, the UK Health Security Agency reported. However, overall antibiotic use fell by 15.1% from 2017 to 2021, from 18.8 to 15 daily defined doses per 1000 inhabitants. Resistance to some key antibiotics remains high, said the agency,



with over two fifths of *E coli* (above) bloodstream infections resistant to co-amoxiclav. An initial assessment of the newer antibiotic cefiderocol susceptibility in *E coli* and *Pseudomonas* spp bloodstream isolates in England has already identified resistance.

A third get antibiotics without prescription

In a survey by WHO across 14 non-EU countries in Europe, only two thirds of respondents said their last course of antibiotics was obtained with a medical prescription. One in three had used leftover drugs from a previous prescription or had obtained them without a prescription over the counter from a pharmacy or elsewhere. This is at least three times as high as the rate reported among EU or EEA states.

Gun violence

AMA establishes prevention taskforce

The American Medical Association is setting up a taskforce aiming to prevent gun violence, reduce the use of firearms in suicide, and increase collaboration with other organisations in litigation related to firearm safety. Every year more than 45 000 firearm related deaths occur in the US, and until earlier this year the country had seen more than 30 years of congressional inaction on the matter, it said. The US's gun homicide rate is 26 times that of other high income countries.

Cancer care

MPs say UK cannot wait any longer for 10 year plan

Steve Brine, chair of the Commons Health and Social Care Committee, urged the health secretary to publish the government's 10 year cancer plan. After the committee's report into cancer services published last April the government said the plan would set a new vision on how to lead the world in cancer care, including having the right workforce. Brine said, "We cannot wait any longer. Waiting lists continue to lengthen with more and more people holding on for potentially lifesaving cancer treatment to begin."

MEDICINE

The men's football World Cup could prompt a rise in harms of gambling, experts fear

Public health

World Cup risks surge in gambling harms

The Association of Directors of Public Health is urging people to use the occasion of the football World Cup as a prompt to talk about gambling. It warned that the gambling industry, which spends around £500m every year on marketing, as well as events such as the World Cup helped to normalise gambling and would cause a spike in gambling related harms. Greg Fell, the association's vice president, said, "The fact that children and young people are so readily exposed [to gambling] is creating a dangerous cycle where society is increasingly engaging with pursuits that can have very real and harmful consequences."

Vaping is best quitting aid, says Cochrane

Electronic cigarettes or vapes are more effective at helping adults to quit smoking than traditional nicotine replacement methods such as patches and chewing gums, a Cochrane review of 78 studies involving 22 052 adults who smoked has found. An additional four people in every 100 could be helped to quit by using nicotine e-cigarettes rather than nicotine replacement, it calculated. Adverse effects were similar in both groups, but researchers said that e-cigarettes were not free of risk and should not be used by non-smokers, particularly by young people.

Young people get advice on digital media use

The Royal College of Psychiatrists has launched an online resource to help parents and carers encourage healthy use of digital media among young people (bit.ly/rcpsych26nov). It warns that digital media can cause problems such as spending too much time away from family, friends, homework, and sleep; looking at information that might be misleading or potentially dangerous; and being exposed to sexualised or violent images and videos or talking to strangers online. Elaine Lockhart, chair of the college's Child and Adolescent Faculty, said, "We need to teach young people how to cope with all aspects of digital technologies, good and bad, and prepare them for an increasingly digitised world."

Climate

Surgeons advise on sustainable operations

The Royal College of Surgeons of Edinburgh, the Royal College of Surgeons of England, and the Royal College of Physicians and Surgeons of Glasgow published a "green theatre checklist" (below) to help surgical teams work more sustainably. The recommendations aim to reduce the "triple bottom line"

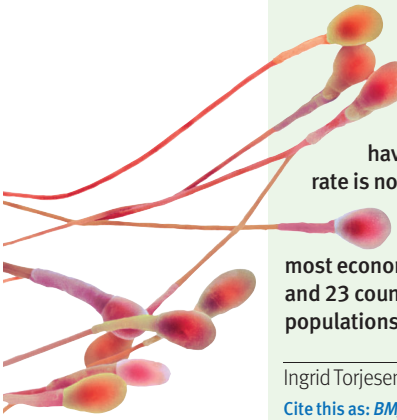
of environmental, social, and economic impacts, they said. Healthcare services account for 4-5% of total carbon emissions, and surgery is particularly carbon intensive. A typical single operation is estimated to generate 150-170 kg of carbon dioxide equivalents, comparable to driving 450 miles (725 km) in an average petrol car.

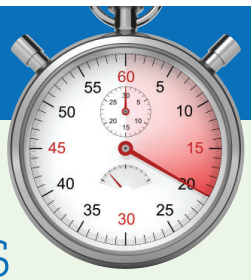
Cite this as: *BMJ* 2022;379:o2808

ALCOHOL

The introduction of minimum unit pricing on alcohol in Scotland led to a fall of **3%** in total sales of alcohol per adult overall: a fall of **1.1%** in Scotland, in contrast with a **2.4%** rise in sales in England and Wales

[Public Health Scotland]





SIXTY SECONDS ON . . . SPERM

NOW YOU SEE THEM, NOW YOU DON'T

Male fertility is falling. Average sperm concentrations have more than halved over the past 45 years, a paper in *Human Reproduction Update* has reported, falling from around 101.2 million sperm per mL of semen in 1973 to around 49 million per mL in 2018.

STILL PLENTY AROUND, THEN

For the moment, yes, but the paper's authors warned that their findings should be seen as a "canary in a coal mine," because if the decline continued it "could threaten mankind's survival." Their meta-analysis showed that the downturn in sperm production was not only long standing but also accelerating. Although sperm concentrations fell by an average of 1.16% a year from 1972 to 2000, since the millennium they have fallen by 2.64% each year.

ARE WE TALKING TIGHT BRIEFS?

It's a bit more complicated than that. Pollution, plastics, smoking, drugs, and chemicals, as well as lifestyle factors such as obesity, poor diet, and lack of exercise, have all been mooted as contributory factors, but the associations are poorly understood. The counting of sperm has also improved, so this may have had some effect. The decline is so serious, however, that it's a significant public health concern, and research is needed on the causes to enable appropriate interventions.

ISN'T EARTH'S POPULATION GROWING?

Yes, but growth is slowing. This month the world's population hit eight billion, having grown by one billion in 11 years, but the UN predicts that it will not reach nine billion till 2037. Then growth is expected to continue to slow and start to decline around 2087.

SO MEN WILL BE TO BLAME?

No, probably women. As a country becomes wealthier and women gain access to contraception, education, work, and freedoms, they have fewer children. The fertility rate is now below 2.1—the level required to maintain a stable population without immigration— in most economically developed countries, and 23 countries are expected to see their populations halve by the end of the century.

Ingrid Torjesen, *The BMJ*

Cite this as: *BMJ* 2022;379:o2805

Funding rises for health and social care will not help patients, say experts

New funding rises for the NHS and social care announced in the chancellor's autumn statement this week will soon be swallowed up, health leaders and analysts have said.

The BMA said rising inflation was set to outstrip the health budget increase at a time when pressures in hospitals, in general practices, and across the healthcare system "have never been greater."

"This failure to match spending with the cost of providing care means services will inevitably be impacted and patients will suffer further," said Emma Runswick, the BMA's deputy chair of council.

The chancellor, Jeremy Hunt, delivering the autumn financial statement on 17 November, said the NHS budget will rise by £3.3bn in each of the next two years, and social care will receive £7.5bn over the next two years. He said this would help free up hospital beds and deliver an estimated 200 000 more care packages over the next two years, one of the biggest increases ever.

This failure to match spending with the cost of providing care means services will inevitably be impacted
Emma Runswick

NHS chief executive Amanda Pritchard said, "While I am under no illusions that NHS staff face very testing times ahead, particularly over winter, this settlement should provide sufficient funding for the NHS to fulfil its key priorities."

Part of the £4.8bn social care funding increase will come from savings made by delaying for two years the introduction of reforms proposed by the economist Andrew Dilnot that would cap individuals' lifetime care costs to £86 000 and to which the government agreed in 2013. The cap was due to come into force next October. Local authorities will also have "more flexibilities" to increase council tax to pay for social care.

Hunt also announced a new drive to find further efficiencies in integrated care systems, to be led by former Labour health secretary Patricia Hewitt. "We want Scandinavian quality alongside Singaporean efficiency, both better outcomes for citizens and better value," he told MPs.

Hunt also committed the government to tackle NHS workforce

NHS BUDGET will rise by £3.3bn in each of the next two years, and social care will receive £7.5bn over the next two years

FIFA concussion protocol was "abject failure," says charity

The brain injury charity Headway has condemned the decision to allow Iran's goalkeeper, Alireza Beiranvand (in blue below), to continue playing after clashing heads with a team mate in the World Cup match against England as an "utter disgrace."

In the first half of Monday's match Beiranvand collided with outfielder Majid Hosseini, which led to the goalkeeper needing treatment from medical staff for several minutes on the pitch. Despite being treated for a head injury and appearing disoriented Beiranvand was permitted to play on, before being substituted a few minutes later after signalling he needed to come off.

After a similar incident in the English Premier League last month Luke Griggs, Headway's interim chief executive, said that stubbornness at the highest level of football was putting players' health at risk. He called for temporary substitutes to be introduced as soon as a player seems to be concussed. "We need to see a change in attitude from IFAB [the International Football Association Board] and FIFA when it comes to brain injury in football," he said.

FADEL SENNA/GETTYIAMGES

"Clearly distressed"

Directly after the England-Iran match Griggs said, "It is an utter disgrace that the Iran keeper was allowed to stay on the pitch. He was clearly distressed and unfit to continue. This seems to be another case of the decision being made by the player and not medical staff. This was the first test of the FIFA World Cup concussion protocol, and it was an abject failure."

It is an utter disgrace that the Iran keeper was allowed to stay on the pitch
Luke Griggs

The Professional Footballers' Association, the trade union for footballers in England and Wales, added, "We have seen a clear example, on the world's biggest stage, of the current concussion protocols not being applied under match pressure."

Last month Headway criticised the decision in an English Premier League game to allow Aston Villa goalkeeper Emiliano Martínez to stay on the field after appearing to have sustained a head injury, before he asked to be substituted. Griggs said at the time, "Team medics are placed in the impossible position of having to make immediate judgments about an evolving condition—with tens of thousands of fans watching them work. It is not an

shortages and to publish next year an "independently verified plan" for the numbers of doctors, nurses, and other professionals that will be needed in five, 10, and 15 years' time. He said this would take full account of the need for better retention and productivity improvements.

Workforce needs

NHS Providers, the King's Fund, and the NHS Confederation said that the £3.3bn funding rise for the NHS showed the Treasury had heeded warnings from NHS leaders that the service was "on its knees" and welcomed the independently verified assessment of NHS workforce needs.

Saffron Cordery, NHS Providers' interim chief executive, said, "We must not forget this announcement follows years of underinvestment in which health spending has fallen below that of comparable European countries.

"The impact of double digit inflation and deep budget cuts to other key public services will exacerbate the cost of living crisis and consequently pile on the pressure on the NHS."

Jeremy Hunt, the chancellor, delivers his autumn statement

But there was disappointment that Hunt failed to act to mitigate the punitive pension taxes that force many senior doctors into retiring from the NHS. "The chancellor himself recently described the situation of doctors being forced to retire early due to these absurd tax arrangements as a 'national scandal,' yet today he has chosen not to take any action to end it, as is now well within his power to do," said Runswick.

Matthew Limb, London

Cite this as: *BMJ* 2022;8360:o2791

US approves drug that delays type 1 diabetes

The FDA has approved an immunotherapy treatment for type 1 diabetes that can delay the onset of the condition by up to three years in adults and children aged at least 8 who have stage 2 type 1 diabetes.

Tzield (teplizumab-mzwv), delivered by intravenous injection once a day for 14 days, works by binding to certain immune system cells to delay progression to stage 3. The treatment may deactivate the immune cells that attack insulin producing cells, while increasing the proportion of cells that help moderate the immune response.

This week saw the launch of the UK based Elsa (Early Surveillance for Autoimmune Diabetes) screening trial, co-funded by Diabetes UK and the JDRF, which is seeking to identify children at high risk of type 1 diabetes.

Colin Dayan, professor of clinical diabetes and metabolism at Cardiff University School of Medicine, who leads the UK Type 1 Diabetes Immunotherapy Consortium, said the US approval of Tzield the treatment "adds weight" to the value of screening for type 1 diabetes. "Ultimately, I hope it will lead to needing insulin to treat type 1 diabetes in childhood being a thing of the past," he said.

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2022;379:o2798

appropriate or effective way of making a clinical judgment."

He said that "If in doubt, sit it out!" was supposedly at the heart of concussion protocols in all sports but that too often the decision was "Let's see how they get on for the next 15 minutes," during which time they risk "exacerbating the effect of the initial injury."

In a statement FIFA said it had implemented a "comprehensive concussion protocol" in the match in which team doctors are encouraged to remove players with suspected concussion from the field.

A spokesperson said, "While the ultimate responsibility in terms of concussion diagnosis and management lies with the relevant team doctor, FIFA expects all teams to act in the best interests of their players and their health."

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2022;379:o2818

Doctors express scepticism over GMC's letter of "reassurance" on referrals

Advice intended to reassure doctors that the GMC will take working conditions into account when dealing with any referrals it receives during the "difficult" winter ahead has been met with scepticism.

In a letter co-signed by four UK chief medical officers, the CQC, and England's national medical director, the GMC said doctors may need to "depart from established procedures to care for people" in the coming months and they may be "fearful that they will be referred." But it said that, in that "unlikely event," the GMC will take "local realities and the need to adapt practice at times of significantly increased national pressure" into account.

But some doctors were sceptical given the treatment of Hadiza Bawa-Garba and Manjula Arora. Their GMC cases caused major upset over the treatment of doctors from ethnic minority groups and those who trained overseas.

Asangaedem Akpan (right), a consultant geriatrician in northwest England, said, "I truly believe our senior colleagues who have written these letters believe what they have written and are individuals with credibility and integrity. However, as a person of colour I have no confidence that I or any clinician of colour will be treated fairly or the same as a white clinician.

"This is because the system is institutionally racist and discriminatory, and until such a time when it is reformed so that everyone is treated the same way I do not trust the referral process to be fair."

Data show doctors from ethnic minorities were twice as likely as white doctors to be referred to the GMC by their employers for fitness to practise concerns. The referral rate among doctors qualifying outside the UK is three times that of UK doctors.

The MDU and MDDUS said GMC actions must match its words. Naeem Nazem, of MDDUS, said, "What is needed now is more practical support to help doctors get through this winter."

Elisabeth Mahase, *The BMJ*

Cite this as: *BMJ* 2022;379:o2800

COVID-19: **Is the UK still tracking the virus—and other questions**

With the NHS braced for a tough winter, **Elisabeth Mahase** looks at what's happening with covid tracking and testing, and variants

MARK KERRISON/ALAMY

Are we still tracking covid cases?

Although the UK significantly scaled back its covid surveillance earlier this year, the Office for National Statistics's coronavirus infection survey, which involves an online questionnaire and swab and blood samples, and the Real-time Assessment of Community Transmission (REACT-1) study both continue.

The ZOE covid study was also given additional funding by the Department of Health and Social Care for England in June this year to continue its work on tracking cases and symptoms. This study relies on a smartphone app in which members of the public can log their symptoms daily.

Are people still being tested?

Outside these surveillance studies, the public can no longer get a covid-19 polymerase chain reaction (PCR) test from the NHS, with the government instead directing people to shops and pharmacies where they can buy a test. Some people are still able to get free rapid lateral flow tests, if they are going into hospital or work in health or social care. Also, testing still takes place in hospitals and for vulnerable people who are eligible for treatment in the community.

What does this mean for tracking new variants?

While mass testing has largely stopped, the testing described above does allow for some sequencing and therefore some ability to track variants. The latest report from the UK Health Security Agency of cases sequenced between 2 and 8 October 2022 showed that 87.4% were BA.5, 5.5% BA.2.75, 4.5% BA.4.6, 0.6% BA.4, and 0.5% BA.2, with 1.5% "other." The HSA has also flagged two new variants: XBB recombinant and BQ.1.

XBB, a recombinant lineage composed of two BA.2 parent lineages, BJ.1 and BM.1.1.1, was first raised as a signal during monitoring on 11 October. Between 16 and 24 October a total of 1104 samples were uploaded to GISAID (the global open access genomic database) from 28 countries across five continents. Most samples (639, 58%) have been uploaded from Singapore, but 18 English samples have been uploaded.

Meanwhile, BQ.1, a BA.5 sublineage, was first raised as a signal on 12 September. Notably, this subvariant has a spike mutation (R346T) on a site that has been associated with a growth advantage. As at 24 October 2022 a total of 3207 samples had been uploaded to GISAID from 48 countries, across six continents, with the highest prevalence in the US (1060) and UK (717).

The latest reports indicate that BQ.1, alongside another omicron lineage variant, BQ.1.1, have now become dominant in the US. Together they make up around 44% of new SARS-CoV-2 infections there, while BA.5 now accounts for just 30%.

Is the UK heading for another covid surge?

The ONS infection survey and the government's covid-19 dashboard indicate that cases and hospital admissions are actually declining at present.

In the week ending 8 November an estimated 1.73% of people in England (one in 60) tested positive for SARS-CoV-2, a decrease from 2.43% the previous week. In Northern Ireland around 1.86% of the population (one in 55) people tested positive, down from 2.17% the previous week; and in Scotland this figure was 1.85% (one in 55), a decrease from 2.04%. In Wales, in the week ending 9 November, an estimated 1.84% (one in 55) people tested positive, down from 2.38% the previous week.

Meanwhile, hospital admissions have continued to decrease in most regions in England, from an average of 5.37 per 100 000 to 5.00 per 100 000 in the week ending 13 November. Deaths mentioning covid-19 have remained stable, with 650 registered in the week ending 4 November, one fewer than the previous week. However, all deaths registered in England and Wales remain above the five year average, with around 1517 excess deaths.

How are the covid and flu vaccine booster programmes going?

In the two months since the autumn 2022 booster programme launched, 15 million of 26 million eligible people have so far had their covid booster, NHS England has reported. Meanwhile, more than 14 million have also already had their flu jab. Vaccination sites are offering both vaccines at the same time where suitable, with a vaccine administered to each arm.

To boost uptake NHS England sent out reminders earlier this month to a million people who have not yet had their vaccines. In addition, local pharmacists in the East of England have produced a series of videos in languages commonly spoken in the region in an attempt to reach people from ethnic minority groups.

Do people still have to isolate now the UK is "living with covid"?

Current NHS guidance advises that people who have tested positive for SARS-CoV-2 try to stay at home and avoid contact with other people for five days. It says that for 10 days they should also avoid meeting people who are at an increased risk from serious illness from covid.

For people who have not been tested, the guidance says those with symptoms, a high temperature, and who do not feel well enough to go to work or carry out normal activities should "try to stay at home and avoid contact with other people."

IN ENGLAND

an estimated **1.73%** of people tested positive in the week to 8 November, down 0.7 points on the previous week

? How are clinically vulnerable people coping with the government's strategy?

NHS advice to clinically vulnerable people is still to carry on with many of the measures that previously applied to the whole population. These include continuing to wear a face mask in shops, on public transport, and when it's hard to stay away from other people and to stay at least 2 m away from others. Additionally, it says to work from home where possible and to meet people outside if possible.

However, many clinically vulnerable people have been frustrated at the lack of consideration for them in the government's plan for living with covid-19, especially considering the lack of preventive treatments that have been made available. A key example of this was the government's decision not to supply the monoclonal antibody Evusheld, which many countries already use as a pre-exposure prophylaxis to prevent covid-19 in people who have moderate to severe immune compromise. This decision is somewhat supported by NICE, which said in draft guidance published on 16 November that it wasn't currently recommending Evusheld for treating people who already have covid-19, citing concerns over cost effectiveness and a lack of evidence of effectiveness against omicron variants, though it will review it separately for preventive use.

NICE is not recommending Evusheld for now, citing cost effectiveness concerns and lack of evidence

Commenting on NICE's guidance, Stephen Griffin, associate professor at the University of Leeds, said, "If we limit the options available for such therapies, especially potential prophylaxis, then we are leaving those most vulnerable to infection high and dry, given the unmitigated prevalence and multiple waves we are experiencing at present."

Elisabeth Mahase, *The BMJ*

Cite this as: *BMJ* 2022;379:o2802

NHS England's backlog recovery is at serious risk, watchdog warns

NHS England's plan to reduce long waiting lists for elective care by 2025 is at serious risk, the government's spending watchdog has warned. A report from the National Audit Office, published on 17 November, found major workforce problems, productivity at a lower level than before the covid pandemic, and funding that has not kept pace with inflation.

It follows a delayed plan from NHS England, published in February 2022, which set out how it would deal with backlogs and long waiting lists over the next three years.

The sharp increase in elective activity expected by NHS England to meet its goals—which involves reaching 129% of 2019-20 levels—would be an "historic feat," the report warned. Even if it were achieved, NHS England has not been able to show it would be enough to meet the commitments set out in its plan, the NAO said. And there are many risks and challenges threatening to push recovery further off track, including unfilled posts, worsening staff morale, and widening health inequalities.

In its previous report on waiting times, in 2021, the NAO noted that the NHS had not met elective care standards for four years or targets for cancer services for eight years.

So far in 2022-23, overall elective care has been below the planned trajectory, the new report said, partly because of circumstances that have proved tougher than assumed, with covid-19 continuing to put pressure on services. Some progress has been made on the longest waits of more than two years, but the overall waiting list has continued to increase and now stands at seven million patients, it noted.

The report also raised concern about the limited evidence of effectiveness for some initiatives within the recovery plan, including use of advice and guidance systems and surgical hubs and community diagnostic centres.

The Department of Health and Social Care and NHS England should review the progress of the recovery plan in early 2023-24 to decide whether targets and funding allocations need to be adjusted and to more clearly define how activity and long waits are measured, the NAO concluded.

Gareth Davies, its head, said, "There are significant risks to the delivery of the plan to reduce long waits for elective and cancer care services by 2025.

"The NHS faces workforce shortages and inflationary pressures, and it will need to be agile in responding as the results of different initiatives in the recovery programme emerge."

Meg Hillier, chair of the House of Commons Committee of Public Accounts, said that fixing NHS backlogs was a "monumental challenge" and that the committee had previously warned against overoptimistic plans. "Patients will continue to suffer the consequences if NHS England doesn't act now to improve its management of the programme," she said.

Urgent referrals from GPs for cancer were up 15%, but figures up to August showed that only 62% of patients began treatment within 62 days, whereas before the pandemic the figure was 78%, the report said. In all, 26 of England's 42 integrated care systems have said they will not reach their 2022-23 target of delivering 104% of pre-pandemic elective activity

Siva Anandaciva, chief analyst at the health think tank the King's Fund, warned that the report should ring alarm bells in government. "NHS funding is not keeping pace with inflation, plus staffing shortages and covid-19 cases in the wider health and social care system are still endemic—all of which put government targets to reduce hospital waiting lists in jeopardy."

An NHS spokesperson said that the NHS was currently on track to deliver on its next recovery plan milestones, after already virtually eliminating waits longer than two years for care and reducing 18 month waits by almost 60% in a year.

"Staff have achieved this despite higher staff absences, more covid patients in hospital this summer than the last two combined, reduced hospital capacity caused by social care issues discharging patients back into the community, and increased demand on urgent and emergency care services," the spokesperson said.

Emma Wilkinson, Sheffield

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THE BIG PICTURE

Doctors targeted in Iran as police seek protesters in hospitals

Doctors in Berlin took to the streets earlier this month to show solidarity with peers in Iran who find themselves on the front line against the country's theocratic regime.

In the most serious incident so far a young surgeon was killed and several more doctors injured on 26 October when police opened fire on a demonstration outside the Tehran Medical Council building. The doctors were protesting against the police presence in hospitals that are treating people injured in increasingly violent public protests.

As protests enter a third month, more than 300 people have been killed by security forces, 15 000 have been arrested, and five death sentences have been pronounced. The protests began when Mahsa Amini, 22, was killed by morality police for violating hijab laws.

The refusal of the top medical official in the southern province of Hormozgan to certify police claims that Amini had died from a heart attack sparked the current unrest. Attributing the death to head trauma, Hossein Karampour wrote to the head of the Iranian Medical Council, Mohammad Raiszadeh, a government appointee, urging him to act "with honesty and courage to clarify and reveal the truth."

Raiszadeh refused. This brought him a rebuke in a letter from 800 members of the medical council, who wrote that he had abused the council's reputation and had forgotten the "moral and social obligation of doctors to defend the people."

The medical council's president and vice president, both assaulted by police during the October protest, resigned the next day. Another council member had been arrested the previous day, along with several prominent doctors across the country. The number now in custody is unknown.

Owen Dyer, Montreal

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OLAF SCHUELKE / ALAMY

EDITORIAL

Maternity service failures in East Kent

Preventing these recurring tragedies requires a highly coordinated system level response

The report into failings in maternity and neonatal services in East Kent Hospitals University NHS Foundation Trust is the latest in a horrifying series of investigations into maternity care.[1]

Led by Bill Kirkup, it yet again bears painful witness to the anguish of families. The outcomes in half (97) of the 202 cases reviewed would have differed had care been given to nationally agreed standards. Many of the deaths (45 of 64) and brain injuries (12 of 17) in babies could have been avoided, as could most maternal deaths and injuries (23 of 32). Beyond these grimly countable outcomes, women experienced many indignities, and families who sought understanding and redress were often exposed to further trauma.

The failings' origins are multifactorial and cumulative, arise from a complex tangle of behaviours and systems in dysfunctional settings, and evade detection and effective action over long periods.[2] It is, however, organisational and institutional failure to tackle unacceptable practices and behaviours over more than a decade that is an especially egregious feature of East Kent.

One important problem was that unprofessional behaviours by some consultant obstetricians were not tackled. Some consultants did not attend labour ward rounds, review women in labour, draw up care plans, or attend the hospital on request when they were on call. Although the Royal College of Obstetricians and Gynaecologists identified such behaviours as a major problem in its 2016 report on the trust, it seems they may have played a role in the death of baby Harry Richford in 2017.

The trust seems to have been supine in dealing with the problem, apparently believing it would probably lose at an employment tribunal if it took disciplinary action against consultants. It is unclear whether this perception is grounded in evidence. In addition, the GMC declined to initiate fitness-to-practise proceedings in 2020 on the grounds that its role did not extend to "lower-level behavioural issues, or cultural issues, or attitudinal issues," indicating a surprising ambiguity about what counts as reasonable concern. Regulators and national agencies need to work together to review employment and case law, contracts, and national standards to produce clear integrated guidance on how to deal with such matters within the current complex ecosystem of local and national bodies.

The failure to tackle unacceptable practices and behaviours over more than a decade is an especially egregious feature

Mary Dixon-Woods, director, THIS Institute, University of Cambridge
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Defective HR procesess

Bullying, harassment, and discrimination were endemic at East Kent. Management systems, including human resources processes, seem to have been seriously defective. For example, bullying and harassment policies at the trust—in a possible misinterpretation of the Advisory, Conciliation and Arbitration Service (ACAS) guidance—required people raising concerns to speak with the subject of the complaint informally. This was a deeply misguided approach, since the trust comprehensively failed to ensure that it was safe to do so.

Particularly disturbing is the evidence of racial abuse in the report, with the trust rated one of the worst in the country for workplace diversity and attitudes towards cultural difference. Again, HR processes seem to have been unfit for purpose.

The systems that might have supported psychological safety, including people feeling safe voicing concerns, were weak or absent.[3] Staff were deterred from speaking up for fear of retaliation (which in some instances seemed to be justified). They were then perversely blamed for their lack of courage, with trust leadership responding to anonymous concerns in 2014-15 by saying nothing could be done "if no one is brave enough to put their name on these letters." It is in fact possible to investigate anonymously raised concerns. But it is also the case the guidance on how best to do so could be much improved, with ACAS likely to be the right body to take this forward.

A 2014 investigation concluded that the trust's bullying problem was so bad one of the units should be shut down because of the risk to women. But diagnoses are useless unless effective treatment follows—and that requires leadership commitment and sound systems,[4] both of which East Kent lacked.

At its most fundamental, East Kent was a system failure. The organisation's weaknesses in tackling poor conduct, behaviour, and culture arose from defects in its leadership and management (especially HR processes), but the wider context was also important. When the trust was clearly unable to handle the situation—or even properly recognise that it was happening—there was no effective mechanism to take over.

The chillingly recurrent discovery of the same failings in report after report in maternity care and elsewhere represents an unforgivable forgetting of painful lessons.[5] Stopping another repeat will require a system level, highly coordinated response that deals with the overlaps and underlaps of the multiplicity of bodies and confusions about their authority and responsibilities[6]—as well as vastly improved management systems in NHS organisations. It will also require sound, evidence based approaches to improvement that genuinely involve staff and patients.[7]

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EDITORIAL

Public health cuts hit the poorest hardest

Funding must be restored to save lives and reduce inequalities

Despite excellent evidence that investing in public health and prevention saves lives,[1 2] the UK government has failed to support such investment. The 2021 spending review made clear commitments to maintain local authority funding for the public health grant in real terms until 2024-25,[3] but higher than expected inflation means it is already set to fall in 2022-23.

The public health grant is a ringfenced allocation of funds made to English local authorities by the Department for Health and Social Care. It is used to provide vital preventive services for local populations, including for smoking cessation, drug and alcohol problems, children's health, and sexual health.

Falling budgets

In 2022-23, the allocation was £3.4bn (€3.9bn; $3.9bn) across England.[4] The largest areas of planned spend were on services for children aged 0-5 years (£0.9bn, mainly on health visitors for infants and mothers), drug and alcohol services for adults (£0.7bn), and sexual health services (£0.6bn).

A Health Foundation report published at the end of October showed that the public health grant has been cut by 24% in real terms per person since 2015-16.[4] Some of the largest reductions were for stop smoking services and tobacco control (41% real terms cut), drug and alcohol services for adults (28% cut), and sexual health services (23% cut). The report also showed the unequal level of spending on public health and the NHS: government spending on NHS England has increased in real terms over the past decade.

A review by the University of Cambridge, also commissioned by the Health Foundation, found a considerable body of evidence showing the effectiveness and cost effectiveness of public health and preventive interventions, including those funded by the public health grant.[5] Research included in the Cambridge review shows that each additional year of good health (measured in quality adjusted life years (QALYs)) achieved by public health interventions costs just £3800.[1] This is less than one third the cost of each additional QALY achieved through NHS interventions (£13 500).

Protecting people's health through timely preventive measures helps to reduce economic inactivity

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Poor health is strongly associated with socioeconomic deprivation. A girl born today in one of the 10% most deprived areas is expected to live 19 fewer years in good health than a girl born in one of the least deprived areas. However, real term cuts to the public health grant have disproportionately fallen on more deprived areas. Cuts in Blackpool, one of the most deprived local authorities in England, were among the deepest in the country—£42 per person in real terms since 2015-16.

Opportunities to prevent early deterioration of people's health are clearly being missed, while the need for such interventions is increasing rapidly. Failure to invest in vital preventive services such as smoking cessation will worsen population health and widen health inequalities still further. The increased costs of dealing with the consequences will be felt across all sectors of society and the economy. Protecting people's health through timely preventive measures helps to reduce economic inactivity[6] and increase the number of people in work.

A properly funded public health system is urgently required, alongside a coordinated strategy prioritising public health and health equity, across all government departments. But the signs are not good. The government has repeatedly failed to publish its promised white paper on health inequalities, for example.[7]

Smoking cessation

In 2019, the government pledged to make England "smoke free,"[8] defined as population smoking rates of 5% or less. Given the deep cuts to smoking cessation services it is unlikely this ambition will be delivered. Smoking cessation programmes improve the health of individuals and can also have a substantial effect on household budgets.

These services are more critical than ever in the current cost-of-living crisis. The average cost of smoking 20 cigarettes a day is £4841 a year. Smoking is highly addictive, and the likelihood of quitting successfully can be increased up to threefold with the help of behavioural support and drug treatment, according to data collated by Action on Smoking and Health.[9]

Health professionals, patients, and the wider public should send a clear and urgent message to the health secretary, the chancellor of the exchequer, and the prime minister: if you care at all about improving people's health and reducing health inequalities, restore the £1.5bn[3] that has been cut from to public health funding in recent years. This would save lives and reduce inequalities.

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Three ways genomics is already helping NHS patients—and three ways it will soon

Four years since its launch, the Genomic Medicine Service is delivering on its promise to transform patient care, reports **Claire Ainsworth**—with much potential still to be realised

England's chief scientific officer is effuse in her praise of the "new era of genomic medicine" we are in. "It's transforming patient care across cancer, rare diseases, diabetes, heart disease, and so much more—including for seriously ill babies—through faster and more accurate diagnoses, more effective and targeted treatments, and helping to predict and prevent conditions developing," says Sue Hill.

In the two decades since the first draft of the human genome was published, genomics has been synonymous with the future of medicine—one tantalisingly close and yet always seeming intangible to most patients and doctors.

The NHS Genomic Medicine Service, launched in 2018, was intended to change that by embedding genomics in routine clinical care. Hill says it is "transforming the tools that clinicians have to deliver better care for patients—whole genome sequencing (WGS), large panels for cancer, RNA sequencing for rare diseases, and more—which is giving them more information about their patient's condition and how best to treat them."

The service hit the headlines in October with the announcement of the launch of a national rapid WGS scheme for babies and children who are seriously ill or born with a rare disease. NHS chief executive Amanda Pritchard hailed the moment as a "global first" and "a new era of genomic medicine." The same day, NHS England launched its five year genomics strategy.

Here are some of the ways the technology is already embedded in the NHS and benefiting its patients, and some of the ways it is likely to in the near future.

The service is transforming the tools clinicians have to deliver better care
Sue Hill

Genomic medicine in action

The clinician-patient relationship is changing through things like genomics
Jillian Hastings Ward

Faster and more democratic diagnosis of rare disease

There are about 7000 rare diseases, most are genetic. While they may be individually rare they are collectively common, affecting some 400 million people around the world. Genomic tests such as rapid exome sequencing (sequencing of the protein coding regions of genes) and WGS, now available through the NHS, are finding answers for patients and giving a diagnostic yield of up to 30% in some cases, says Hill.

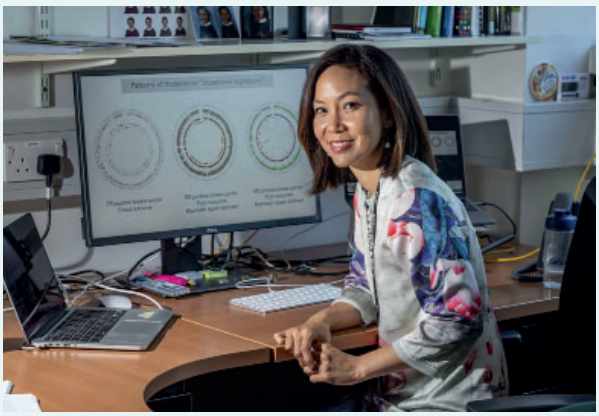
The effect has been transformative for many patients. Ten to 15 years ago, affected children were referred to specialist clinical teams who could spot patterns in symptoms and either offer advice or order targeted tests. "Clinically, the team had to come up with something closer to a diagnosis and it needed therefore to be something that they knew about," says Richard Scott, consultant in clinical genetics at Great Ormond Street Hospital in London, who sees children with complex medical problems of unknown cause.

Genomic medicine allows teams to short circuit the conventional diagnostic process and diagnose much more quickly and broadly, says Scott, who is also chief medical officer at Genomics England. Even the best experts in the world can struggle to diagnose with clinical skills and routine tests alone. "The bottom line for families is that more people are getting diagnoses, and earlier, so they don't have to go through this very long diagnostic odyssey that people talk about," he says.

This faster diagnosis also means that patients with rare diseases and their families can find each other more quickly, says Jillian Hastings Ward, whose son Sam was diagnosed with a rare genetic condition called GRIN1 thanks to the 100 000 Genomes Project. This helps patients form support groups and work with scientists and clinicians to accelerate the development of new treatments for these conditions, says Hastings Ward, who also chairs the Genomics England participant panel, an advisory group that ensures that the experiences of patients and their families are included in Genomics England's work. "The traditional clinician-patient relationship is changing through things like genomics. It's becoming much more of a team sport than a one way channel of information," she says.

It's sparking more optimism in clinicians, too, says Scott. "You almost become accepting of the challenges," he says. But the arrival of big technologies can suddenly reveal the potential to change things for families. "And that's really exciting."

There is still progress to be made: 20%-40% of patients receive a genetic diagnosis, and Genomics England is now investigating the use of methods that study proteins and RNA to try to raise diagnosis rates, says Parker Moss, chief ecosystems and partnership officer at Genomics England.



Whole genome sequencing can be used to improve the design of clinical trials Serena Nik-Zainal

A more holistic view of tumours

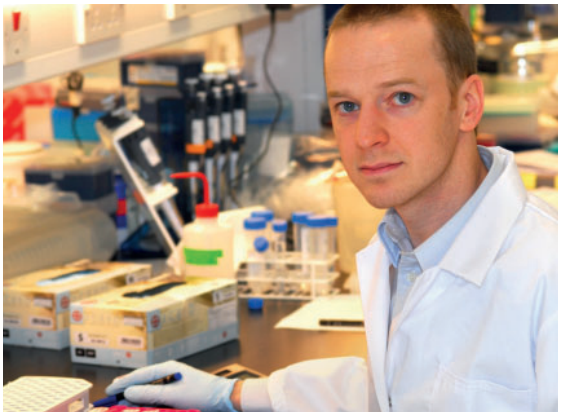
NHS cancer patients can already benefit from genomics in the form of sequencing of a panel of genes to identify key mutations that are targeted by particular anticancer treatments. The NHS is working to standardise its cancer sequencing around 500 genes, says Moss. But even so, he says, these are only part of the picture and WGS, which covers 22 000 genes and also the non-coding regions of the genome, is being rolled out. All children in the UK with cancer are now eligible for WGS through the national test directory, as are adults with sarcoma and some acute leukaemias. Breast and ovarian cancers are likely to follow.

WGS lets doctors take a more holistic view of a tumour. It can help them identify patients who are relapsing at a much earlier stage than was previously possible. At the Genomics England Research Summit 2022 in May, Jack Bartram, a consultant paediatric haematologist at Great Ormond Street Hospital, described 10 cases in which WGS had helped not only with diagnosis but also with management, such as helping doctors decide which children needed a bone marrow transplant as well as chemotherapy, and identifying potential targeted therapies in advance to save time in case of relapse. "We know from genome-wide studies that there is more to the picture than we're doing at the moment with standard-of-care diagnostics," Bartram told the conference.

The same is true for adult cancer patients. Serena Nik-Zainal, a clinical geneticist at Addenbrooke's Hospital in Cambridge and a professor of genomic medicine and bioinformatics at the University of Cambridge, has identified patterns of mutations, known as mutational signatures, across the genome in cancers. The signatures reflect the DNA damage and repair processes that have occurred during the development of a tumour. Different signatures correlate with predicted sensitivity to different drugs, allowing doctors to develop better targeted, effective treatments for individual patients.

In 2017 Nik-Zainal and her team sequenced the whole genome of a man with terminal angiosarcoma, and uncovered a mutational signature indicating the tumour would be sensitive to checkpoint inhibitors, drugs that strip a cancer of its ability to hide from the immune system. The patient responded well to therapy. Nik-Zainal has also used the method to show that nearly 1 in 5 patients with breast cancer (and more than 1 in 2 triple negative patients) have deficiencies in a pathway involving the genes BRCA1 or BRCA2, even if the genes themselves are not mutated. Such tumours are likely to be sensitive to DNA damaging drugs such as platinum and poly (ADP-ribose) polymerase inhibitors.

WGS can also be used to improve the design of clinical trials, says Nik-Zainal. Both Nik-Zainal and Bartram say, however, there is some resistance among oncologists to adopt WGS in their clinical practice—partly because the standard of care diagnostics are so good, but also because it demands more resources, time, and training. But help is on its way: Nik-Zainal's team, for example, is developing tools to make the interpretation of WGS results quicker and easier.



Covid-19: Finding the vulnerable—and those who might benefit from drugs

"The use of genomic sequencing in tackling the covid pandemic was a proof point on an international scale of the potential for genomics to revolutionise healthcare," says Hill. "It allowed us to track outbreaks, identify new variants, and, through projects like the Genetics of Mortality in Critical Care (GenOMICC) study, we are able to analyse why some people experienced mild symptoms while others had a severe reaction."

The power of genomics could uncover factors predisposing patients to a severe response to covid-19. The GenOMICC studies compare the genomes of critically ill patients with those of population controls to find underlying disease mechanisms. Earlier this year, a GenOMICC study, led by Kenneth Baillie (above) at the University of Edinburgh in partnership with Genomics England, sequenced whole genomes from nearly 7500 intensive care patients with covid-19 from across the UK.

The study identified 16 genetic variants that made some patients with covid-19 more likely to become critically ill. These included variants within genes involved in immune cell signalling, white blood cell differentiation, and blood clotting. A number of these mechanisms are druggable, highlighting new research hypotheses to explore for potential drug development.

A 2021 GenOMICC study of critically ill NHS covid-19 patients suggested that a drug already in use to treat arthritis, baricitinib, might be used to target a pathway highlighted by one of these gene variants. The protein encoded by this gene is involved in the inflammatory organ damage seen in severely ill covid-19 patients.

Baracitinib was tested as part of the Recovery trial, and in March this year researchers announced that the treatment cut mortality by between 13% and 20%.

These projects involved rapid and extensive collaboration across the NHS and UK research institutions, including intensive care researchers, Genomics England, the NHS, and the NIHR clinical research network, says Scott. "It was a fantastic example of the whole ecosystem in the UK working together, leveraging what we can do and then having the impact that we've seen."

Genomic promise

Newborn genomes programme

Clinicians and many parents in the UK will be familiar with the newborn blood spot test, which screens infants for nine rare conditions that benefit from early treatment. In mid-2023, the NHS and Genomic England hope to take this to the next level, by performing a pilot study of WGS of newborn babies to expand testing to many more rare diseases. If the pilot is successful, WGS for newborns will be implemented into routine NHS care.

The aim of the study is very focused—the NHS will analyse genome sequences only for conditions that emerge during childhood and for which clinical interventions exist, rather than returning every possible bit of information, says Simon Wilde, engagement director at Genomics England. Guidelines such as these are the result of a careful programme of public engagement performed in the light of Genomic England's experience with the 100 000 Genomes Project. Public acceptance is key for the success of the programme, says Wilde.

The team is also consulting rare disease experts to make sure that all the conditions to be reported have treatment pathways and care packages available. "It's about making sure that we've got everything in place before we begin."

The results of the first public dialogue exercise showed that the public are supportive of the technology, as long as certain conditions and safeguards are met. These include data privacy and informed consent (see box, below right). "That's what we've been able to take forward and at least begin to start thinking about: what would a programme of sequencing genomes in babies look like?" says Wilde.

The team is also studying factors such as the best time during pregnancy to approach women with information about the programme. "We need to make sure that the offer we make is one that's acceptable, that's understandable, and that works for parents," says Wilde.

The project will begin next summer and aims to sequence up to 100 000 newborn genomes in the first instance, with the possibility of going beyond that if needed.

Cancer 2.0

Genomics England has recently launched a research programme, in collaboration with the NHS, called Cancer 2.0. "This is not yet clinical, but it has clinical intent," says Moss. Cancer 2.0 has two main aims: to explore new DNA sequencing technologies and to unite imaging data with genomic data, to develop new insights into cancer and improve diagnosis and treatment.

The new sequencing technologies centre on nanopore sequencing, which can read long sections of DNA and so detect changes involving large chunks of the genome that are hard to spot with current "short read" technologies. This is important because "structural variations increasingly look like they are druggable directly," says Moss. It can simultaneously detect DNA methylation patterns that are key to understanding epigenetic contributions to a cancer.

The imaging arm of the Cancer 2.0 project involves integrating radiology and digital pathology images with genome data from the 15 000 cancer patients in the 100 000 Genomes Project. In partnership with Leeds Teaching Hospitals NHS Trust and the National Pathology Imaging Co-operative, the project will create a large dataset of more than 250 000 digital pathology images, alongside detailed diagnostic information from pathology reports.

Combining the molecular features of the tumour with spatial images should give you much more specificity about whether a patient will respond to treatment, says Moss. "Response to treatment to drugs is not always simply dependent on the molecular biology of the tumour, but also about the microenvironment of the tumour," he explains. Applying machine learning to the data should also yield deeper insights into the disease and anticancer treatments. It might ultimately be possible to use these algorithms to diagnose cancers in the clinic.

PATIENT DATA

Data security and confidentiality are sensitive areas when it comes to gaining and keeping public confidence in technologies such as genomic medicine.

Seeking, gaining, and maintaining consent are key, says Wilde. Ongoing public engagement and developing best practices for data management is "a foundational part of what we do," he says, and has been since the inception of the 100 000 Genomes Project. "It's something that we take very seriously. It's something that we know is a live issue and will continue to be a live issue."

Genomics England works on a model where it obtains consent before any data are stored and ensures that people understand what they might be used for, how anonymised they might be, and what security safeguards are in place. "What we'd like to do is try and talk about what the potential risks and benefits might be, but ultimately make sure that people have that choice about whether to take part in the first place," says Wilde. "But if they ever get cold feet or, for whatever reason, they don't want to take it anymore, that there are mechanisms in place for them to have their data removed and destroyed."

Personalised prescribing

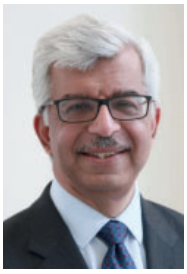
How well a drug works, the risk of adverse side effects, and what the optimal dose is can vary considerably between patients. Much of this variability is affected by genetics, and researchers have identified variants affecting patient response to more than 40 drugs. Testing for these variants, known as pharmacogenomics, is still limited within the NHS. But moves are under way to expand the range of tests available, and even to take a proactive approach that involves testing patients before they need treatment and recording the results for future reference, says Munir Pirmohamed, a clinical pharmacologist, and David Weatherall, chair of medicine at the University of Liverpool.

A small number of genetic tests for adverse drug reactions are already available on the NHS, including HLAB57 testing for hypersensitivity to the anti-HIV drug abacavir, and dihydropyrimidine dehydrogenase (DPD) deficiency to prevent serious toxicity from a class of anticancer drugs known as fluoropyrimidines. This identifies patients who should receive lower doses of the drugs to minimise adverse side effects.

But there is a clear need to expand these tests to cover more drugs. What's more, an increasing number of drug manufacturers are stipulating genetic testing on their medicines to guide dosing. Some of these tests are not available on the NHS and must be done privately. "It is important we think about how we can make sure to make that available because people will develop adverse effects that we could have prevented," says Pirmohamed. Being better able to predict drug efficacy will help clinicians avoid trial and error when treating some conditions like depression and select the best drugs faster. "Even if it increases the predictability a little bit, then we may reduce some suffering for our patients," says Pirmohamed.

Pirmohamed's own work shows just how dramatic this reduction can be. In 2004, his team showed that genetic testing for abacavir hypersensitivity was cost effective. By 2006, all NHS HIV clinics were using the test and hypersensitivity rates dropped from 5%-7% to less than 1%.

Instead of single gene tests, Pirmohamed and his colleagues are advocating panel tests, where patients are typed for a range of variants and these are kept on the patient's electronic health record. "You've already got the data available rather than having to do it again," he says. His team is working with Our Future Health, a forthcoming research programme that aims to recruit five million UK residents. Pirmohamed's team has designed the gene chip that will be used to type participants for pharmacogenomic variants. Ethical discussions are still under way, but it is possible that the data will be returned to individual participants.



Patients need to understand what the advantages are, but also the limitations
Munir Pirmohamed

Another project to which Pirmohamed is contributing, UP-Gx, recently ran the Preemptive Pharmacogenomic Testing for Preventing Adverse Drug Reactions trial, which recruited 6900 people from across Europe, including patients from the Royal Liverpool University Hospital. The study pre-emptively tested participants with a panel of 40 markers in 13 genes associated with drug responses. Doctors used this information when prescribing drugs for patients in the test group (those in the control group received standard care) with the aim of reducing adverse drug reactions. The data from the study are now under review at a medical journal.

The field is not without obstacles: like many other genomics projects, phamacogenomics suffers from a lack of ethnic diversity in its study subjects. For example, the NHS currently tests for four variants in the DPD gene, but these variants are all derived from European ancestry populations, says Pirmohamed. There are no tests for rare DPD variants in patients with African backgrounds, meaning they might wrongly be classed as wild-type. Pirmohamed is currently working on a project in the UK and internationally to identify more of these variants in a range of ethnicities. He also has a project under way to develop genetic testing for warfarin dosing in populations in sub-Saharan Africa.

Ultimately, a patient's whole genome sequence could be kept on record and then interrogated for phamacogenomic data, says Pirmohamed. But patients need to be involved in the design of these services. "They need to understand what the advantages, but also the limitations, are," he adds. Delivering pharmacogenomics also means creating clinical decision support systems so that busy primary and secondary care clinicians don't have to spend a lot of time trying to decipher genetic test results, he adds. Another matter is applying pharmacogenomics to people taking multiple drugs, a particular problem in elderly patients.

Pirmohamed sees pharmacogenomics as an evolution, rather than a revolution, in clinical practice. "The way I look at it, the predictivity that we have at the moment is pretty low," says Pirmohamed. "If we can achieve an increase in predictivity for particular drugs to more than 50%, more than 60%, then we're doing a much better job than we are at the moment."

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THE BMJ INTERVIEW

Will New Zealand be "smoke free within three years"?

The country wants to become the first to create a "smoke-free generation," by banning the sale of tobacco to anyone born after 2008. **Charlotte Lytton** asks Ayesha Verrall, associate minister for health, whether this "bold" plan is on track to succeed

As a doctor I'd admit people to hospital suffering the harms of cigarettes

The intention to become "smoke free" by 2025 was announced in 2011. Why have efforts ramped up now?

"I came into office as associate minister of health in 2020, and it was apparent that we needed to take bold action to reach that goal. At that point our smoking rate was 11%. It's now 9%, so we need to change what we're doing to reach that target."

Why are you personally committed to this cause?

"I've been a doctor until just recently. During most of my 20s, as a house officer and registrar, I'd spend my night and evening duties admitting people to hospital suffering the harms of cigarettes. In particular, I looked after a lot of people with chronic obstructive pulmonary disease, who had come to hospital out of breath in distress, fearing that it was so hard to breathe they would die. And this would happen to them repeatedly throughout the course of a winter. It was a miserable way to watch people die, because tobacco had harmed them."

People of European ethnicity are on track to reach the target, Māori and Pacific Islanders aren't. We need to all get there together

How likely is it that you will have a smoke-free generation in three years?

"The smoke-free generation policy, which is just one of three measures we're putting in the legislation, is the first of its kind. But it is also possible because of the point in time New Zealand is at: we have low rates of youth smoking. This is essentially about using two other policies—'denicotinisation' and retail outlet reduction—to support people to quit, and then the smoke-free generation policy consolidates our smoke-free status for years to come."

What are the biggest challenges threatening that goal?

"Our goal was also that each ethnicity in New Zealand should reach a 5% smoking prevalence for their population. We knew there were marked disparities, and there still are. So while New Zealanders of European ethnicity are on track to reach the target, Māori and Pacific Islanders aren't. We need to make sure we all get there together."

Why are the disparities so great?

"There are multiple types of social disadvantage that make it difficult to quit for low income people, Māori, and Pacific people. If we just talk about recent history, over the past 10-15 years one of the primary tools we've used to reduce smoking rates has been excise tax increases. New Zealand now is one of the most expensive places to buy cigarettes. Counterintuitively, the people who quit smoking under that policy were more likely to be higher income and Pākehā (white New Zealanders) . . . I think it shows one of the complexities of dealing with an addictive substance, and perhaps the people with less control or choice in their lives find it harder to quit in that way."

How will the ban be enforced?

"It is the retailers who are prohibited from sale: we are not putting sanctions or any offences on the people who are purchasing, so addicted people don't get driven into criminal networks by needing to get tobacco."

What role does vaping play?

"We want vapes to be available to support quitting. In the previous year we had our largest ever drop in smoking, and that may be due to the availability of vapes."

Do we know enough about vaping's long term safety for it to be encouraged?

"I'm very aware that we don't want young people to see vaping as a primary new thing to do, outside of that role as supporting quitting. So if we have to relook at our regulations [around vaping] and tighten them, we have that option.

"Almost anything is a better alternative than a product that kills half the people who use it. I think it is clear that vaping is less harmful than tobacco. I think what is unclear is precisely what the long term impacts of vaping are. That's why we see it as a quit tool and not something we encourage people to start from."

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