this week

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LEON NEAL/GETTY IMAGES

Cut workload to tackle GP crisis, MPs told

The unsafe workload of GPs needs to be reduced to prevent an exodus of doctors, MPs have been warned.

In the opening session of the Health Select Committee's inquiry into the future of general practice, GPs said the pressures of workload and poor job satisfaction were causing many to retire early and making it hard to fill vacant posts.

Last year the GMC reported that, of all the medical professions, GPs were continuing to report being under the greatest pressure of burnout, with a third saying they were likely to quit in the coming year. And a BMA survey found that two thirds of GPs aged over 55 intended to retire within three years.

Andrew Green, a GP who retired recently aged 58, told MPs that while he had enjoyed the job for 30 years the pressure of high workloads and too little time to see patients had prompted his early retirement. "We need to accept that 10 minute appointments are not safe. The only way that you can have a 10 minute appointment surgery on time is by cutting corners," he said. "One of the things that made me finally give up was the feeling at the end of the day that I wasn't happy with the work that I'd done, because I couldn't fit in what the patients needed."

Green said that such a level of pressure takes its toll on GPs' mental health. "It makes you leave, because you come home at the end of the day worrying."

Kate Fallon, a GP partner in Somerset, told the committee her practice had not been able to recruit a GP despite advertising since last July. "When I first went into medicine, we had 30 plus applicants per post. We've never put out an ad and had nobody interested. It's having a huge impact on the three partners who are left," she said.

Martin Marshall, chair of the Royal College of General Practitioners, said there was no doubt the profession was in crisis. "I've been a GP for just over 30 years, but I've never seen things as low as they are now," he said. "There has to be hope for general practice otherwise there's no hope for the NHS. We need to be working really hard on long term solutions now."

He added that the main solution was a larger workforce, but that less bureaucracy and politicians communicating honestly with patients would help in the short term.

Becks Fisher, GP and senior policy fellow at the Health Foundation, highlighted the need to attract younger doctors with "tangible improvements to our working lives."

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2022;376:o684

Martin Marshall, RCGP chair, warned that the situation for general practice was the worst he had seen in 30 years

LATEST ONLINE

- Government has overseen "years of decline" in cancer and elective care, say MPs
- Johnson & Johnson "regrets" 1971 study that injected asbestos into US prisoners
- Opioid lawsuits: Sackler family agree final $6bn civil settlement with US states

SEVEN DAYS IN

England saw record 4.3 million referrals to mental health services in 2021

The Royal College of Psychiatrists has urged the government to publish a fully funded recovery plan for specialist mental healthcare in England in response to the "unprecedented demand" driven by the pandemic.

The college's analysis of NHS Digital data showed a record 4.3 million referrals to mental health services in England between January and December 2021, with 3.3 million referrals to adult mental health services and just over a million to under-18 services.

The data show 1 834 137 appointments were attended across mental health, learning disability, and autism services in December 2021, 14.7% higher than two years earlier.

The college noted that 1.4 million people were currently waiting for treatment and called on the government to urgently publish a plan to reduce waiting times, backed by funding to expand services, train more psychiatrists, and replace inadequate facilities.

The college's president, Adrian James (left), said, "The warning of the long tail of mental ill health caused by the pandemic has not been heeded. Many thousands of people will be left waiting far too long for the treatment they need unless the government wakes up to the crisis that is engulfing the country." **(See Opinion, page 442)**

Gareth Iacobucci, *The BMJ* **Cite this as: *BMJ* 2022;376:o672**

Cancer

Views are sought on proposed new standards

The NHS launched a consultation on proposed new standards that aim to help diagnose more cancers earlier and are based on recommendations from the Independent Cancer Taskforce. Cancer currently has nine performance standards, with targets covering routes into the system, such as screening or GP referral. The new proposals include the 28 day faster diagnosis standard to see patients who have been urgently referred, have breast symptoms, or have been picked up through screening; a 62 day standard from referral to receiving treatment; and a 31 day standard from the decision to treat to the patient receiving treatment.

Ukrainian children arrive in UK for cancer treatment

Twenty one Ukrainian children arrived in England on 13 March to receive cancer treatment. They will be triaged by NHS clinicians to understand their health needs before being sent to NHS hospitals to continue their care. NHS England's chief executive, Amanda Pritchard (right), said, "The situation in Ukraine is deeply shocking and saddening, and the NHS will continue to help in any way we can, whether that is by working with government to provide medical supplies directly to Ukraine or, in this instance, by making sure these children get the crucial treatment they need."

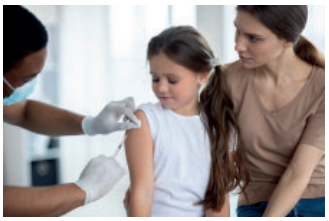
Vaccines

WHO backs "urgent and broad access to" third jab

The World Health Organization updated its guidance on covid vaccine booster shots and is now recommending them. Last year WHO called for a moratorium on boosters, arguing they contributed to vaccine inequity when many people in poorer countries had yet to receive a first shot. In January it softened that position, saying boosters were recommended once countries had adequate supplies and after protecting their most vulnerable people. After reviewing vaccine availability it has now said it "strongly supports urgent and broad access" to booster doses to combat the omicron variant.

NHS offers booster to the most vulnerable children

The NHS will shortly invite 4400 children aged 12-15 who are most at risk from covid in their age group to book their booster



online. The government accepted advice from the Joint Committee on Vaccination and Immunisation last year to extend boosters to include children receiving chemotherapy or radiotherapy and those with leukaemia, diabetes, chronic diseases, or severe mental illness.

Covid-19

Public inquiry terms of reference are published

The government published the terms of reference for the public inquiry into the handling of the pandemic. The wide ranging terms cover national and local public health responses, government decisions, and much more. In the NHS it will examine areas such as infection prevention and control, triage, critical care capacity, patient discharge, the use of "do not attempt cardiopulmonary resuscitation" (DNACPR) decisions, the approach to palliative care, the impact on staff, the management of the pandemic in care homes, and procurement of PPE and ventilators.

Government withdraws funding for symptoms app

Researchers behind the leading covid symptoms study by the healthcare company ZOE and King's College London said they were "incredibly disappointed" the UK Health Security Agency had opted not to renew their funding. Since March 2020, 4.7 million users have used the smartphone app to report symptoms and covid test results. Tim Spector, cofounder and scientist at ZOE, said, "ZOE has been at the forefront of critical scientific discoveries which have saved lives. We believe not renewing the funding is a huge mistake for the UK and science."

Global deaths are "more devastating" than thought

The first peer reviewed study of global excess deaths, published in the *Lancet*, estimated that 18.2 million excess deaths occurred from 1 January 2020 to 31 December 2021, far more than the official figure of 5.9 million. The study compared average death rates from before the pandemic to calculate excess deaths in 74 countries and territories. The authors said that evidence from initial studies suggested that a significant proportion of excess deaths were a direct result of covid but more research was needed.

MEDICINE

Homeopathy

Impact is "substantially overestimated"

Poor research practice may mean that the true impact of homeopathy is substantially overestimated, said an evidence review published in *BMJ Evidence Based Medicine*. Many clinical trials have not been registered, 38% remain unpublished, and the main outcome was changed in a quarter of those published. All of this indicated a "concerning lack of scientific and ethical standards and a high risk for reporting bias," said the researchers. They added that journals publishing homeopathy trials did not adhere to international standards, which say that only registered studies should be published.

Clinical trials of homeopathy have a "concerning lack of standards"

Climate crisis

Welsh hospital's solar farm helps reduce bills

The £5.7m Brynwhillach solar farm in southwest Wales, the UK's first solar farm owned by a health board, supplied Morriston Hospital in Swansea with 100% of its energy needs over a single 50 hour period, the Welsh government reported. The 4MW project has saved an estimated £120 000 in electricity bills since it was switched on in November and is projected to save 1000 tonnes of carbon emissions and £500 000 a year when fully operational. It has also sold back 30 000 kWh of surplus energy to the energy grid at a profit to the hospital.

Transplantation

Teenager with autism gets kidney go-ahead

A High Court judge ruled that William Verden, 17, who has autism, attention deficit/hyperactivity disorder, and a complex learning disability, should be approved for a kidney transplantation despite Manchester University NHS Foundation Trust originally deciding that it would not be in his best interests. Verden has kidney failure and had steroid resistant nephrotic syndrome (SRNS) diagnosed in December 2019. The court heard that if SRNS recurred after the transplantation he would need to have plasma exchange requiring sedation and ventilation for as much as 14 days, which carried many risks, including post-intensive care syndrome. But Mrs Justice Arbuthnot decided that the transplant would not be futile.

Otitis media

NICE: consider anaesthetic and analgesic ear drops

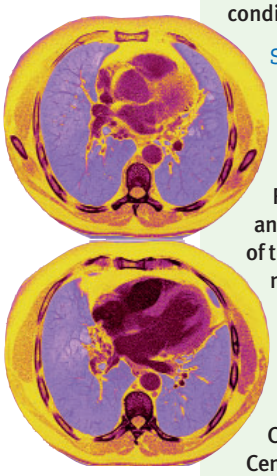
Ear drops containing an anaesthetic and an analgesic should be considered for cases of acute otitis media when an antibiotic is not indicated and there is no ear drum perforation or otorrhoea, NICE said in updated guidance, to further reduce overuse of antibiotics for this condition. An estimated 60% of the 896 000 cases of acute otitis media in children aged under 5 in England could be treated with the ear drops rather than oral paracetamol or ibuprofen, which are routinely used.

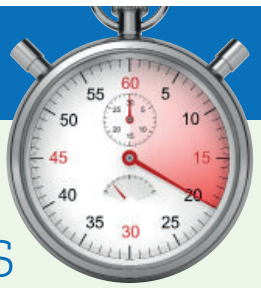
Cite this as: *BMJ* 2022;376:o673

TRAINEES

791 medical students have been placed on the reserve list for the 2022 UK foundation programme, up from 494 in 2021 and 258 in 2020. The NHS in England is currently short of 8158 doctors

[Health Education England, NHS Digital]





SIXTY SECONDS ON . . . AI HEART CHECKS

WHAT'S THIS ALL ABOUT?

A new artificial intelligence tool can detect heart disease at record speed and could even help cut the NHS backlog, says the British Heart Foundation, which funded the research. A study published in the *Journal of Cardiovascular Magnetic Resonance* found that the tool analysed cardiovascular MRI scans more precisely than three clinicians.

JUST HOW QUICK IS IT?

The AI can analyse heart scans in 20 seconds while the patient is still in the scanner. In comparison, it would typically take a doctor 13 minutes to analyse images after the scan.

THAT'S SPEEDY, BUT IS IT ACCURATE?

The programme detects changes to heart structure and function with 40% greater accuracy and extracts more information than a human can, the study found. The algorithm was trained to measure the thickness of the heart muscle, the size of the left ventricle, and how well the heart was able to pump blood. The algorithm was based on MRI scans from 1923 people, with seven heart conditions, at 13 hospitals and using 10 models of scanner. The AI was then validated on a further 109 twice scanned patients.

HOW WILL IT BE USED?

The AI was designed to diagnose a heart condition when someone is initially assessed. It can also spot early signs of heart disease. The researchers hope to develop it further so it can quantify heart valve disease and congenital heart defects. The tool can also help doctors see how patients with heart conditions are responding to treatment.

SO, THE NHS BACKLOG?

Around 120 000 heart MRI scans are performed each year in the UK. The hope is that the AI could help fast track diagnoses and ease workload. Rhodri Davies, study leader at the UCL and Barts Heart Centre, said, "The beauty of the technology is that it replaces the need for a doctor to spend countless hours analysing the scans by hand."

IS IT IN A HOSPITAL NEAR ME?

The technology is being used on more than 140 patients a week at University College London Hospital, Barts Health Centre, and Royal Free Hospital. It will be rolled out later this year to 40 sites across the UK and around the world.

Jacqui Wise, Kent

Cite this as: *BMJ* 2022;376:o667

Progress on eliminating racist complaints against doctors is too slow, say leaders

Doctors' leaders have urged the GMC to do more to stamp out racist complaints against ethnic minority doctors and eradicate disadvantage in medical education and training. The call follows the regulator's admission that performance against the targets it set in 2021 to tackle persistent areas of inequality had been mixed.

A GMC report shows that the proportion of designated bodies with fitness to practise referrals that were disproportionate in terms of ethnicity or UK versus international qualification fell from 5.6% in the five year period to 2020 to 5.3% in the five years to 2021. The gap in employers' fitness to practise referral rates between ethnic minority licensed doctors and white doctors fell from 0.28 percentage points (0.30% white versus 0.58% ethnic minority) during 2016-20 to 0.24 percentage points (0.26% white, 0.50% ethnic minority) during 2017-21.

The GMC will continue our sustained focus, and we are calling on other organisations to do the same Charlie Massey

Charlie Massey, GMC chief executive, said these findings were good early indications of progress. In addition, the GMC itself had improved the ethnic representation of its staff at all levels, which was a key aim.

But measures of fairness in medical education and training remained "essentially unchanged," the report found.

Ramesh Mehta, president of the British Association of Physicians of Indian Origin, said he was disappointed to see so little progress, given the evidence of the extent of inequalities. "We appreciate it's a longstanding problem that can't be solved very quickly, but, unless there is a strong will to use powers and enforce recommendations, things will not change," he said.

Name the officers

Mehta said that the GMC should publicly name the "racist" minority of responsible officers who were referring ethnic minority doctors unfairly and disproportionately. "That will carry a lot more weight than telling the ROs they need to be understanding of cultural background," he told *The BMJ*.

Massey accepted that more must be done, saying, "We will continue our sustained focus, and we are calling on other organisations to do the same."

The GMC set targets to eliminate

Hospital admissions rise as covid cases surge in over 55s

In most areas of England admissions were still below their January peak, but in the south west they rose 37% (from 878 to 1206) last week and were higher than at the peak of the omicron wave. London saw a 27% increase (801 to 1017) in the week to 8 March

England saw a rise in covid related hospital admissions in the week to 8 March, as a study showed that covid cases were rising among people aged over 55, prompting warnings from experts that the pandemic was not over.

Latest hospital data from NHS England show that covid related admissions, which had been falling since the beginning of January, rose by 22% across England in the seven days ending 8 March, from 6894 to 8431.

Admissions rose in all seven regions of England during that week. Colin Angus, a senior research fellow and modeller at the University of Sheffield, said on Twitter, "This trend points to a genuine increase in covid prevalence in recent weeks, most likely connected to some combination of BA.2's growth advantage over BA.1 and the removal of restrictions and a resulting shift in people's behaviour, with greater mixing."

Primary diagnosis

NHS data up to 8 March showed that, while the seven day average number of hospital beds in England occupied by patients with covid rose 1% from 7950 to 8045, those occupied by people with covid as the primary diagnosis actually fell by 2% from 3610 to 3523.

Angus noted that in the south west the big rise in covid admissions was "almost entirely driven by these 'incidental' covid diagnoses."

Meanwhile, the latest findings from the Real Time Assessment of Community Transmission (React) study covering 8 February to 1 March showed that covid-19 prevalence was 2.88%. This compared with 4.41% in January but was the second highest recorded since the study began in 2020.

And while prevalence fell in under 17s and 18-54 year olds during February, there was an increasing incidence in the over 55s.

Paul Elliott, director of the React programme from Imperial's School of Public Health, said, "It's encouraging that infections have been falling across England, but they are still very high and the possibility that they are rising in older adults may be cause for concern.

It's important to follow public health guidance to avoid further spread of the virus Paul Elliott

"The good news is that this is a highly vaccinated group. However, a high number of infections will lead to more people becoming ill, so it's important that people continue to follow public health guidance to avoid fuelling further spread of the virus."

Elliot said that the government's funding for the programme would cease at the end of March, so there would be just one more round of data.

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2022;376:o654

Ramesh Mehta: "Unless there is a strong will to use powers, things will not change"

disproportionate numbers of complaints from employers regarding a doctor's ethnicity and place of qualification by 2026 and to eliminate discrimination, disadvantage, and unfairness in undergraduate and postgraduate medical education and training by 2031.

The fact that there had been little change in terms of fairness in education and training was "not unexpected" given that these outcomes "reflect a complex interplay of inequalities over a 10 to 15 year period in which a doctor is training," the GMC said.

Chaand Nagpaul, BMA council chair, said the lack of improvement in postgraduate differential attainment was "disappointing" and that NHS leaders should be held accountable for ensuring fair processes and ending disparities. "This report brings us no closer to the cultural transformation that is desperately required," he said.

Matthew Limb, London

Cite this as: *BMJ* 2022;376:o648

Scotland's staffing plan criticised

Plans to plug critical gaps in Scotland's health and social care workforce could be undone because of a serious omission, doctors have warned.

A workforce strategy announced by the Scottish government focuses on recruitment and training to deliver sustainable staffing levels but devotes little attention to policies that can help to retain existing staff.

Bernie Scott, deputy chair of BMA Scotland said, "It takes a long time to train doctors—yet at the moment we face the pressing risk of losing more and more of those we have. We need much more coordinated, urgent action now to guard against the possibility of losing many doctors before new recruitment has any chance of making an impact."

Action is needed to make NHS Scotland a better place to work Bernie Scott

The strategy set out plans to increase the NHS workforce by1800 full time posts—equivalent to a 1% increase—over the next four years and an extra 800 GPs by 2028. Figures will be published later this year for required workforce growth, which will be reviewed annually.

Initiatives aimed at meeting the targets will include spending £11m to launch international recruitment campaigns and to establish a Centre for Workforce Supply, increasing medical school places by 500, and investing £230m a year in nursing and midwifery training.

But with consultant vacancies running at over 15% of all posts in Scotland and a nursing vacancy rate of 8.2% (5761 unfilled posts) there is disappointment more is not being done to help existing staff.

Scott described the measures as a mixed bag. He said action was needed on fairer rewards, fixing pension tax changes, a better work-life balance, and "just making NHS Scotland a more attractive place to work, with an improved culture and less of a focus on targets and blame."

Bryan Christie, Edinburgh

Cite this as: *BMJ* 2022;376:o674

GPs get update on treating refugees arriving from Ukraine

GPs have received updated guidance on providing healthcare to people arriving from Ukraine.

In a bulletin to general practices on 10 March notifying them of the update from the Office for Health Improvement and Disparities, NHS England said refugees and citizens returning from Ukraine had begun to seek services and reminded practices that proof of identity was not required for registration.

The guidance advises practices to explain to people how the NHS works and their entitlements to access services, to ensure they are up to date with the UK immunisation schedule, and to ask about any travel plans they may have.

The NHS England bulletin said, "Newly arrived individuals will need help on how to access the NHS, and this will include GP registration as the principal route for accessing services.

"We remind [GPs] that individuals may struggle to provide proof of ID, address, or confirmation of immigration status and their registration requests should be managed sensitively. None of these documents are required for registration, and the inability of any individual to provide them is no reason to refuse registration."

Gareth Iacobucci, *The BMJ* Cite this as: *BMJ* 2022;376:o671

ADVICE TO GPs

- Screen all new entrants, including children, for tuberculosis
- Ascertain any risk factors for hepatitis B that may indicate a need for screening (owing to its low prevalence in the UK)
- Consider screening for hepatitis C, because of a considerably higher prevalence in Ukraine than in the UK
- Ensure that travellers are offered typhoid immunisation and advice on preventing enteric fever
- Consider nutritional and metabolic concerns (anaemia, vitamin D, vitamin A, iodine)
- Work with a professional interpreter where language barriers are present
- Consider the effects of culture, religion, and gender on health
- Assess for mental health conditions
- Refer pregnant women to antenatal care

NEWS ANALYSIS

Ukrainian conflict calls Russia's covid-19 vaccine diplomacy into question

The war has marked a new chapter in the saga of Sputnik V—a vaccine intertwined with geopolitics, reports **Serena Tinari**

Although Russian covid-19 vaccines are licensed in more than 70 countries, their success on the international market could be impeded by the conflict in Ukraine and the onset of global sanctions against the Kremlin.

Sputnik V, a vaccine created at the Gamaleya National Centre of Epidemiology and Microbiology, was developed, promoted, and financed by the Russian Direct Investment Fund (RDIF). On 28 February the US Department of the Treasury included the RDIF in its list of sanctioned Russian entities, and the Council of Europe and several national executives worldwide promptly followed.

The Russian fund responded with a public statement pointing out that the restrictions would complicate its efforts to promote covid vaccines internationally. The RDIF accused "large western pharmaceutical companies" of piggybacking the crisis to achieve a market advantage, underlining that the fund "was never involved in any political activities, does not interact in any way with Ukraine, and follows the world's best investment practices."

Sputnik V, also known as Gam-COVID-Vac, is based on two common cold virus (adenovirus) vectors delivered separately in two doses, combined with the SARS-CoV-2 spike protein. It was later followed by Sputnik Light, essentially only the second component, and more recently by Sputnik M for adolescents, which is currently licensed only in Kazakhstan.

Data criticism

The Sputnik vaccine first made news in August 2020 when Russia's president, Vladimir Putin, announced the country had authorised a "safe and effective" covid-19 biologic. This was before phase 1 or 2 data had been published and before a phase 3 trial had begun. The Gamaleya vaccines continue to face criticism for a lack of transparency in clinical trial documents.

The *Lancet*'s publication last September of the results of two open, non-randomised phase 1/2 studies was met with scepticism, particularly by a group of international researchers who contested the results. The authors defended the solidity of their work and suggested that individual participant data would have been made available on request, which until now has not happened.

Vasiliy Vlassov, vice president at the Russian Society for Evidence Based Medicine, told *The BMJ* that not much has changed since then. Vlassov has been vocal in expressing his reservations about the Sputnik vaccine's methodological issues and on the need for a more transparent approach. He said that although the phase 3 trial had been completed, "a formal final report wasn't published," adding that no field data on Sputnik's safety were apparently collected in Russia.

Vlassov said that "the role of arguments beyond science was very significant in all aspects of the pandemic," with politics and geopolitics also influencing public health affairs.

"At least in part it is a result of insufficient volume of knowledge, a permanent delay in knowledge acquisition in the course of the epidemic, and highly subjective decision making," he said.

In February 2022 Argentina's Ministry of Health granted conditional approval to the Sputnik vaccine manufactured by a local producer, Richmond. Such technology transfer is also taking place in other countries. Commercial details are not disclosed in any of the nations involved, but the Argentinian initiative could effectively open the door to further export of the Sputnik vaccine in other South American countries.

ARGENTINA has stockpiled enough Sputnik V and is rolling out many covid vaccines. More than 79% of the country's population has now been fully vaccinated

International response

Argentina's Ministry of Health told *The BMJ* that no distribution issues were expected despite the international crisis, as Argentina had stockpiled enough Sputnik vaccines and was rolling out many covid vaccines. More than 79% of its population has now been fully vaccinated.

Reuters reported that most of the Indian subcontractors that are soon expected to start producing Sputnik's vaccines had declined to comment on how the crisis would affect the Russian vaccine.

The European Medicines Agency began a rolling review of Sputnik V a year ago, and the World Health Organization had planned to carry out onsite inspections in Russia this month. WHO has not yet granted Sputnik an emergency use listing, which would allow for the vaccine to be included in the Covid-19 Vaccines Global Access (Covax) initiative that distributes doses in lower income countries. It seems likely that any inspections would be on hold, pending developments in Ukraine.

An EMA spokesperson said, "The Sputnik V vaccine remains evaluated under rolling review, although there is currently no active review cycle. We are not commenting any further on ongoing assessments."

In a quickly changing situation it is hard to assess the potential impact of the international crisis on the availability and rollout of the Russian vaccines. Politico has reported that the RDIF has explicitly called for peace in Ukraine—a statement that *The BMJ* was not able to independently confirm.

Serena Tinari, freelance journalist, Bern, Switzerland
Cite this as: *BMJ* 2022;376:o626

Ukraine war: the global research community reviews its links with Russia


Vaccine diplomacy
China, India and Russia seize on Covid jabs in battle for global influence

The Russian development fund accused large drug companies of piggybacking the crisis to achieve a market advantage

WHO has not yet granted the Sputnik its emergency use listing, which would allow it to be included in the Covax scheme

Universities and academic journals around the world are urgently reviewing their links with Russian scientists after the invasion of Ukraine, although views differ on whether collaboration and publishing should be banned outright.

Scientists from Ukraine have called for a complete boycott of the Russian academic community, including banning Russian citizens from being authors or reviewers on international journals, and suspending all funding of and international collaboration with Russian institutions. An open letter, signed by more than 6000 scientists from Ukraine and worldwide, calls on the scientific community to institute wide ranging academic sanctions, including blocking access to science databases and materials and banning Russian scientists from conferences.

On 4 March the European Commission suspended cooperation with Russian institutions involved in research and innovation projects funded by the EU.The commission announced that it would not conclude any new contracts or any new agreements with Russian organisations under the Horizon Europe programme—the EU's key funding programme.

Mariya Gabriel, a European commissioner, said, "Russia's military aggression against Ukraine is an attack on freedom, democracy, and self-determination, on which cultural expression, academic and scientific freedom, and scientific cooperation are based. As a result, we have decided not to engage into further cooperation projects in research and innovation with Russian entities."


THIS IS AN ATTACK ON DEMOCRACY, ON WHICH SCIENTIFIC FREEDOM AND COOPERATION ARE BASED Mariya Gabriel

Germany was the first EU country to announce a blanket ban on research cooperation. The Alliance of German Science Organisations said its funds would no longer benefit Russia, no joint scientific events would take place, and no new collaborations would begin.

Denmark has followed Germany's example, with its research minister writing to universities to urge them to "suspend any research and innovation cooperation" with institutions in Russia and Belarus. Norway said all agreements with Russia were now on hold. In Boston, the Massachusetts Institute of Technology terminated its 11 year partnership with Skolkovo, the innovation hub near Moscow.

In contrast, others have called for academic ties to be preserved. The Belgian Rectors Conference published a statement urging governments to "make sure academic cooperation can continue as much as possible as it allows the free flow of thoughts even during the darkest hours of armed conflict."

Other countries are still considering what action to take. The UK government has said its Department for Business, Energy and Industrial Strategy is carrying out a "rapid review" of Russian beneficiaries of funding.

A statement by Universities UK, said, "We do not support the application of blanket academic boycotts that prevent academics collaborating as a means of protest against the actions of their governments. We are therefore advising our members to make decisions about whether to continue collaborations on a case-by-case basis, informed both by UK government guidance and appropriate due diligence."

It added that education and research partnerships were often based on peer-to-peer relationships and noted many Russian students and academics had publicly criticised the invasion. Several thousand scientists in Russia signed an open letter opposing the invasion despite the career risks and possible imprisonment. The letter says, "Having unleashed the war, Russia doomed itself to international isolation, to the position of a pariah country. This means that we, scientists, will no longer be able to do our job normally: after all, conducting scientific research is unthinkable without full cooperation with colleagues from other countries."

Responses within academia also vary. The editorial board of the *Journal of Molecular Structure* has temporarily banned the publication of studies from Russian institutions, although not of individual Russians.

Many other journals, including *Nature* and *The BMJ*, have said they will continue to consider manuscripts from researchers anywhere in the world.


A BAN IS A ROAD TO A REDUCTION IN THE QUALITY AND VISIBILITY OF RUSSIAN SCIENCE Vasiliy Vlassov

A *Nature* editorial said, "Such a boycott would do more harm than good. It would divide the global research community and restrict the exchange of scholarly knowledge—both of which have the potential to damage the health and wellbeing of humanity and the planet."

In an editorial published last week *The BMJ*'s editor in chief, Kamran Abbasi, wrote, "By boycotting Russian research . . . we risk further marginalising Russian scientists already bravely speaking for peace. We also potentially do harm to Russian civilians, many of whom are protesting against the war."

Commenting on the decision by some publishers to reject Russian submissions, Vasiliy Vlassov, an epidemiologist at the National Research University Higher School of Economics in Moscow, told *The BMJ*, "Of course, it is met with disappointment, but many scientists understand the reasoning. Most scientists are pleased to see that, while institutional collaborations are stopped, many universities and labs continue to support individual collaborations."

Vlassov said that over the past 15 years the Kremlin had promoted the integration of Russian science with the rest of the world and had encouraged publication in international journals.

"Despite the quality of Russian journals improving in the last 10 years, [an international ban] is a road to a reduction in the quality of research and visibility of Russian science."

Jacqui Wise, Kent

Cite this as: *BMJ* 2022;376:o637

THE BIG PICTURE

Hope of new life in the tragedy of war

As the war in Ukraine enters its fourth week, the fate of Mariana Vishegirskaya offered one small ray of hope.

The Ukrainian woman was pictured being evacuated from a maternity hospital near the besieged city of Mariupol (left) after it was hit by Russian airstrikes on 9 March. A day later, after being transported to a second hospital, she gave birth to a daughter, Veronika (above). Both are reported to be doing well.

The UN has reported 596 deaths, including 43 children, and 1067 injuries among civilians in Ukraine as of 13 March. The actual toll is expected to be considerably higher.

Alison Shepherd, *The BMJ*

Cite this as: *BMJ* 2022;376:o669

EVGENIY MALOLETKA/AP/SHUTTERSTOCK

EDITORIAL

Molnupiravir's authorisation was premature

Regulatory decisions fall short of the wise stewardship required during a pandemic

On 1 October 2021 Merck issued a press release[1] reporting an interim analysis of Move-Out, a placebo controlled trial in unvaccinated adults with confirmed SARS-Co-V infection and mild-to-moderate symptoms outside hospital. The press release stated that molnupiravir, a nucleoside analogue that inhibits viral replication by mutagenesis, reduced risk of hospital admission or death by about 50% (P=0.0012) in the 29 days after infection.

The UK Medicines and Healthcare Products Regulatory Agency (MHRA) gave molnupiravir conditional marketing authorisation on 4 November 2021, based on the interim data underlying the press release.[2] On 23 December, the US Food and Drug Administration (FDA) granted emergency use authorisation after seeing the trial's full dataset.[3] These authorisations, conducted behind closed doors, lack adequate scientific rigour, inhibit further necessary evaluations, and may ultimately lead to suboptimal resource allocation decisions.

Both emergency use and conditional marketing authorisations have a lower bar for efficacy than standard approvals. This raises questions about the strength and certainty of the evidence.

Move-Out was stopped prematurely for reasons that aren't completely clear. When the trial was published, the authors reported a smaller absolute difference in primary outcome (−3%, 95% confidence interval −5.9 to −0.1, P=0.043)[7] than quoted in Merck's earlier press release (−6.8%, P=0.0012). The published results have borderline significance, indicating that even a small number of misclassified outcomes could overturn the findings.[8] Robustness is further undermined by a modified intention-to-treat analysis that excluded 25 patients after randomisation.

LAKSHMIPRASAD S/ALAMY

Its mutagenic mode of action could in theory encourage emergence of additional SARS-CoV-2 variants

Prematurely terminated trials are more likely than non-truncated trials to overestimate effect sizes.[9] Interestingly, Move-Out's truncated relative risk reduction (0.5)[1] is 66% higher than the non-truncated relative risk reduction (0.3),[7] emphasising the dangers of making decisions based on a single prematurely terminated trial.

Clinical value?

The real question for any trial is whether the findings are clinically as well as statistically significant. As Move-Out was powered to detect an absolute reduction of 6% in hospital admissions or death, we might reasonably accept this as the minimum clinically meaningful difference. The confidence interval around the published reduction in primary outcome (−3%, 95% CI −5.9 to −0.1)[7] excludes 6%, leading to questions about the clinical importance of these findings.

Molnupiravir's safety profile is also uncertain because Move-Out was underpowered, like most clinical trials, to detect clinically important side effects. Its mutagenic mode of action could in theory encourage emergence of additional SARS-CoV-2 variants. The generalisability of the results is also unclear as the trial population was unvaccinated and recruited before the most recent variants emerged. It is not known whether reported benefits will be maintained across populations with differing variants, ancillary treatments, and healthcare systems. Further uncertainty arises from two more recent studies of molnupiravir reporting no clinical benefit in either outpatients or inpatients with covid-19.[10 11]

Five days' treatment is expected to cost about $700 (£500; €600), and with the manufacturer estimating that demand will reach 10 million courses over the next year,[1] global costs could reach several billion dollars annually. The opportunity costs associated with this agent, including the potential for more financial support for mass vaccinations in low and middle income countries, merit serious reflection.

Detailed cost effectiveness studies by independent health technology assessment groups must be done to avoid repeating past mistakes. Approval of oseltamivir (Tamiflu), an antiviral for early uncomplicated influenza, resulted in worldwide governmental spending exceeding $18bn (half on stockpiling) for a drug with no benefit other than reducing duration of symptoms by less than one day.[12]

The evidence for incorporating molnupiravir into routine practice is fragile. Premature regulatory authorisation and guideline recommendation[13] on the basis of truncated and non-replicated trial findings and without full consideration of clinical significance and cost effectiveness falls far short of the wise stewardship required during a global healthcare emergency. We deserve and should demand better.

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EDITORIAL

UK scales back routine covid-19 surveillance

A walk in the dark

On 24 February, the government removed the legal requirement for people in England to self-isolate after a positive covid-19 test result, with the other UK nations also easing restrictions.[1] In doing so, the UK is acting ahead of many of its international peers to embark on a "vaccines only" strategy, hoping that existing immunity in the population will allow a "return to normal."

This view is in sharp contrast to public opinion. In a recent poll by market research company YouGov, only 17% of respondents thought that ending mandatory self-isolation was appropriate.[2]

The removal of legal restrictions makes the people of England part of an experiment in which much remains uncertain.[3] This is acknowledged by chief government advisers Chris Whitty and Patrick Vallance, who accompanied Boris Johnson's announcement with a warning that rates of covid-19 infection and hospital admission remain high.[4] Of equal concern, the government's announcement also introduced plans to scale back two crucial pillars of the UK's covid-19 surveillance: the Office for National Statistics' (ONS) covid-19 infection survey and daily reporting of data on the UK Health Security Agency (UKHSA) covid-19 dashboard.[1 5] When, and to what extent, these important resources will be scaled back remains unclear. But they will be more important than ever following the recent axing of funds for key UK surveillance studies, including REACT-1.

The ONS survey is a world leading example of random population sampling to estimate covid-19 prevalence over time.[6 7] The UKHSA dashboard has been a vital resource for the public, clinicians, journalists, and researchers, allowing them to identify local trends as well as providing national data.

We need to sustain existing surveillance capabilities until we are certain that the pandemic is over

We remain in the middle of a global pandemic caused by a novel pathogen and complicated by the repeated emergence of new variants. Policy decisions to manage new outbreaks rely on robust and timely data. The alpha, delta, and omicron variants all became dominant in the UK within weeks of the first reported cases,[9] emphasising the need for ongoing vigilance to detect future variants.[10]

Flying blind

From 1 April 2022, when universal free covid tests are withdrawn leaving only limited testing in place, most SARS-Co-V infections in England will remain undetected and unreported. Our ability to track the emergence of new variants or trends in the incidence of infection and disease will become more reliant on robust, cross sectional surveys such as the ONS survey. Scaling back the survey, as proposed, risks missing emerging variants or concerning rises in prevalence that could herald the need for further restrictions. The detrimental effects of delayed action are now abundantly clear, and we must not fall behind at this critical moment.[11]

In announcing the latest relaxation of restrictions, the prime minister asked the public to take individual responsibility for their actions, yet informed decisions are reliant on the availability and accessibility of information. Throughout the pandemic people have relied on regional reporting of covid-19 cases on government dashboards and in news media, and they will continue to need such accessible information for the foreseeable future.

While most people have received two or more doses of a covid-19 vaccine, almost 10% of adults in England have not received a single dose and around 30% have not had a booster.[12] Many others remain at high risk of disease despite vaccination because of underlying health conditions. The public health implications of immunity waning over time remain uncertain.[13 14] As we move into a period of largely optional (and paid for) testing and voluntary self-isolation, it is crucial that people have easy access information to guide their actions and help minimise covid-19 risks to themselves and their families.

The UK has been a world leader in the routine surveillance of covid-19 and the transparent reporting of covid-19 data. Scaling back vital data systems and surveillance studies prematurely is a false economy and may need to be reversed to manage future waves of infection. The UK has the resources and infrastructure to continue existing surveillance, which has clearly identifiable benefits. We need to sustain our existing surveillance capabilities until we are certain that the pandemic is over in the UK, which won't be until covid-19 is controlled globally.

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POLICY

Elections loom large in France's pandemic policies

With national elections weeks away, doctors assess how the French government has managed covid-19, writes **Barbara Casassus**

JEROME GILLES/NURPHOTO/GETTY IMAGES

Doctors in France have mixed views about the government's handling of the pandemic, but they agree that the presidential and parliamentary elections—to be held in April and June—are key factors in setting pandemic policy.

President Emmanuel Macron said in his new year wishes that the pandemic would end this year. Public health took precedence at the start of the crisis, but since the second wave of covid in August 2020, the economy and social pressures have become the focus.

The phased lifting of restrictions in June 2021 marked a big change. "For the first time, a date was chosen without taking account of either the incidence or hospitalisation rates of covid," says Mahmoud Zureik, epidemiology and public health professor at the Versailles-Saint-Quentin-en-Yvelines University.

By then, the vaccination campaign was well under way. Although delta had displaced other variants the previous autumn, the government took "very timid" new measures to contain it, based solely on whether hospitals could cope, says Zureik.

Furthermore, contradictory messages have created confusion. After introducing a health pass (evidence of vaccination, previous infection, or a recent negative test result) for entry to enclosed public spaces this January the authorities upgraded this to just evidence of vaccination or recent recovery from infection. Soon after the new pass had come into force, health minister Olivier Véran was talking about abolishing it "well before July." At the beginning of March, the prime minister Jean Castex said it would be "suspended" on 14 March. Obligatory masks will all but disappear at the same time.

Doctors *The BMJ* spoke to agree that the French government is relying too much on the high vaccination rate, which stood at 74.8% of the population aged 5 and over on 9 March. They regret that preventive measures are being overlooked as the population becomes increasingly weary of restrictions, but falling numbers of covid infections are still high. "With new cases reaching a daily record of more than 500 000 on 25 January, it was illogical to loosen the rules before the fifth wave had peaked," says Jacques Battistoni, president of MG France, the country's largest union of general practitioners. "The government was no doubt more concerned about election prospects than public health."

Restrictions lifted

Djillali Annane, head of the intensive care unit at the Raymond-Poincaré Hospital in Garches, believes the government should have waited until the pandemic subsided at the end of the winter. "We must still be extremely careful," he says. "Hospitals and intensive care units have not yet returned to normal," he told *The BMJ* on 7 March.

Zureik says, "Even though it did not admit it, the government had decided to allow the virus to circulate freely. This is still the case." But Philippe Amouyel, epidemiologist at Lille teaching hospital, disagrees. "The decision has nothing to do with letting the virus circulate freely," he says. "It does that all on its own, and is creating a natural immunity in France and other countries."

The new health pass was intended to encourage rather than impose vaccination. Macron was widely reported as saying he wanted "to piss off" the people who refused to have shots. "Anything that encourages vaccination is good," says Zureik, "but Mr Macron shouldn't have said that. Insults are always a bad idea."

> **The government has never caught up from the catastrophic start**
> Djillali Annane

Battistoni says the numbers of first vaccinations did rise around the time of Macron's remark, but this could be because the vaccination pass was brought in soon after. "I am old school, and think Mr Macron could have made the point another way."

The "purely political" comment was taken out of context, says Amouyel. Macron was responding to the numerous delays to surgery and treatment in French hospitals as increasing numbers of unvaccinated patients were being admitted to ICUs with covid-19.

For Annane, "the worst thing a doctor can do is to try and force a treatment on a patient. It almost always fails." Even though at that point Macron had still not announced he would run for re-election, "he was clearly taking a swipe at the political far right, a hotbed of anti-vaxxers. But this neither surprises nor shocks me."

When asked to assess the government's management of the pandemic, some doctors gave low marks for the chaos at the start, but high marks for its management later.

Battistoni gave a score of 4 out of 10 for the beginning, when there were no masks, no protective equipment for healthcare workers, and no tests. But he would give an 8 now. He is less severe in his assessment than some colleagues, because as a union chief, "I am closer to the difficulties than most. I attend a lot of meetings with the authorities and see how complicated each stage of the pandemic can be."

Annane gave the government a score of 5 overall, as it "has never caught up from the catastrophic start" and has merely replaced initial problems with new ones. Amouyel

KIRAN RIDLEY/GETTY IMAGES

LUDOVIC MARIN/AFP/GETTY IMAGES

Ministers were no doubt more concerned about election prospects than public health
Jacques Battistoni

Clockwise from bottom, President Emmanuel Macron; hospital workers protest in Bordeaux in 2021; travellers show their covid health pass; and election campaign posters

gave 7 out of 10, rising to 8 at times. He credited the government for anticipating the fourth wave in July 2021 and bringing in the health pass to public spaces.

A shift in primary care

Jean-Paul Hamon, honorary president of the Fédération des Médecins de France, which represents non-hospital doctors, raised his rating for the government from 3 out of 10 to 7. One of his biggest gripes at the beginning was the sidelining of community practitioners. "It told patients with suspected covid to ring the general health emergency number rather than their GPs, and to renew their prescriptions for chronic diseases directly with their pharmacists," he says.

The government did not call on unions of non-hospital doctors to discuss the pandemic until 18 February 2020, after Véran had taken over from Agnès Buzyn. Even then, in a two hour press conference, Véran overlooked non-hospital doctors, thanking their hospital colleagues for their hard work and never mentioning that most deaths in doctors from covid were in non-hospital practitioners. "Governments have always forgotten us, but never to this extent," says Hamon.

That changed when vaccinations were rolled out in December 2020, and general practitioners became central to the campaign, he adds. "Even so, there is still a way to go in involving non-hospital doctors and nurses in diagnosis and shortening hospital stays."

Hamon gives the government full marks for adding a child psychiatrist to its advisory scientific council in early 2021, and for not bowing to pressure from some doctors to impose a second strict lockdown when the second wave hit in August 2020. "Mr Macron knew that the French people's morale would not stand it, and the wave turned out not to be as severe as had been feared. It is not easy to govern right now."

Court action

For months, the French government has been under fire for allegedly mishandling the crisis. Legal complaints have flooded in from individuals, patient associations, and medical practitioners. Recently, the Court of Justice of the Republic, which hears cases against ministers in office, threw out nearly 20 000 complaints, all filed at the behest of lawyer Fabrice Di Vizio. Most opposed the health pass and pressure to vaccinate. Targets were prime minister Jean Castex, Véran, education minister Jean-Michel Blanquer, and junior transport minister Jean-Baptiste Djebbari. The public prosecutor has already indicted Véran's predecessor Agnès Buzyn with endangering life, and is conducting a judicial investigation into the performance of Véran and Philippe.

Several doctors single out Blanquer in particular for having bungled the school health measures. "I would give him 2 or 3 out of 10, rather than zero, because the situation is even worse in the UK than in France," says Zureik. The minister "changes the school protocol every five minutes," says Hamon. It was "absurd" not to postpone the new term in January, adds Annane. "There were four different protocols in a week, and since then children have been a huge accelerator in spreading the omicron [variant]."

Vaccine sceptics

Epidemiologist Antoine Flahault, founding director of the Institute of Global Health in Geneva, regrets that the French government has not done more to convince sceptics to be vaccinated. "Portugal and Spain have succeeded in changing their minds, without making vaccinations compulsory, [by] introducing a pass or offering cash incentives," he said.

He also regrets that France has fallen so far behind in vaccinating children aged 5 to 11. "It's a great shame, and is due in part to French paediatricians' traditionally lukewarm attitude to vaccinations," he says. Some French speaking paediatricians believe children with natural immunity are more resistant to infectious diseases in adulthood, says Flahault, citing Jean-François Bach, a member of the French Academy of Sciences, as one scientist behind the theory. These paediatricians recommend vaccinating children against what they consider to be dangerous diseases—poliomyelitis, diphtheria, tetanus, and whooping cough—but oppose vaccination against "benign" diseases such as measles, chickenpox, flu, and now covid-19, in children with no underlying health problems.

At the beginning of the pandemic, children were regarded to be at low risk of complications from covid-19, but now "we know they are easily infected, and can still suffer severe complications, including inflammation and even death," says Flahault. "In Europe, 80% of children hospitalised with mild or even severe forms of covid-19 have no other diseases and seem to be just as vulnerable to long covid as adults are." In France, a study showed that 77% of the 82 children aged under 13 hospitalised between August 2021 and January 2022 had no comorbidities.

Flahault's harshest criticism is against France in the position of EU presidency, and the EU in general, for failing to take a strong lead on air quality. "Now we know that the virus is transmitted by aerosols, it is clear that ventilating enclosed spaces is the key to ending the pandemic," he says.

"Ninety nine per cent of infections occur indoors, and we spend more than 90% of our time indoors."

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BABY MILK SUBSTITUTES

Formula milk companies push allergy products despite flawed evidence

Europe has toughened its approach to formula milk products that claim to reduce allergy risks. But consumers elsewhere continue to be coaxed into buying products that make health claims without high quality evidence. **Melanie Newman** reports

For decades, the formula industry has claimed that certain breast milk substitutes can reduce the risk of allergies, but the science underlying these claims has been largely revealed to be fraudulent or flawed. Yet today, Nestlé and Danone are still advertising those claims in some countries where rates of acute malnutrition, morbidity, and mortality are high and where how babies are fed is critically important.

The World Health Organization has told *The BMJ* that governments should be scrutinising health claims on formula products more carefully. In a highly critical report on formula milk marketing last month, WHO said that the practice represented "one of the most underappreciated risks to the health of infants and children."

The health claims have been made for a type of formula milk called hydrolysed milk, including both partially hydrolysed and extensively hydrolysed formula (box 1).

After heavy campaigning the UK, Europe, and the US have taken steps to clamp down on unevidenced claims that hydrolysed milk products prevent or reduce the risk of allergies. Last year, in a move that the UK has followed, the European Commission prohibited the use of such allergy claims on infant formula unless manufacturers could prove the efficacy of each product. In one case Nestlé was prevented from claiming that a hydrolysed product reduced the risk of eczema in infants with a family history of allergy.

But in other markets, including in China and Russia, consumers are being persuaded to buy expensive formulas that have little evidence of proven benefit for healthy infants. So: what needs urgent attention, how should change be made, and what is the cost of the status quo?

Box 1 | What is hydrolysed formula?

There is no universally accepted definition of a partially hydrolysed formula (pHF) or extensively hydrolysed formula (eHF). Partially hydrolysed proteins are created using enzymatic processes to partially break the proteins into smaller fragments, or peptides. Extensively hydrolysed peptide based formula milks contain proteins that have been extensively broken down or hydrolysed, using pork enzymes.

pHF has been included in formula products intended to reduce the risk of allergic diseases and also to support other claims such as easy digestion. eHF is used in the management of formula fed infants who have cow's milk allergy or other less common intestinal issues such as pancreatic insufficiency or malabsorption.

WHO urged an end to unethical formula milk marketing in a critical report last month

There is little evidence that hydrolysed formula has any role in feeding healthy infants
Robert Boyle

Flawed evidence

Over recent years researchers have gradually debunked most claims that infant formula reduces the risk of babies developing cow's milk allergy and eczema. Most significantly, the tide turned after the retraction in 2015 of a 25 year old study in *The BMJ*, which had found that mothers with a history of allergy should feed their babies hydrolysed formula to reduce the risk of them developing an allergy to cow's milk. Ranjit Chandra, a Canada based researcher who was an author of the study, was investigated by his employer, which concluded that "scientific misconduct" had been committed. But before 2015 his work had been used by the formula industry to kick start a multi-million pound market for hydrolysed infant milks.

A year later, in 2016, the UK Food Standards Agency stated after a systematic review that hydrolysed formulas did not influence the risk of a child developing allergies. At the same time a meta-analysis and systematic review in *The BMJ* found no evidence to support the conclusion of a 2006 Cochrane review that using hydrolysed formula instead of ordinary cow's milk formula could reduce allergies in babies and children.

In 2018 Cochrane updated its review and found no evidence to support prolonged feeding with hydrolysed formula when compared with standard cow's milk formula for preventing allergic disease in infants. It also found "very low quality" evidence that

TOP KIM KYUNG-HOON /REUTERS/ALAMY

short term use of an extensively hydrolysed formula compared with standard cow's milk formula could prevent infant cow's milk allergy. But it recommended further trials before implementing this practice.

Since then, Australia and the US are among the countries that have changed guidelines that previously recommended using hydrolysed formula to prevent allergies. Guidelines that have now dropped this recommendation include the Australasian Society of Clinical Immunology and Allergy and the American Academy of Pediatrics.

In a 2021 paper Robert Boyle, clinical reader in paediatric allergy at Imperial College London, wrote, "Overall there is little evidence that hydrolysed formula has any role in feeding healthy infants." NICE recommends specialist formula only for the treatment of suspected IgE-mediated cow's milk allergy and only when the product is extensively hydrolysed.

***The BMJ* has previously revealed the overmarketing of specialist formula milk for infants**

China is the largest and the most rapidly growing formula market in the world

Under-regulated markets

This growing consensus in the scientific community against the role of formula in allergy risk reduction has not, however, led to the withdrawal of products that make such claims elsewhere in the world.

In China, the largest and the most rapidly growing formula market in the world, Nestlé heavily promotes its NAN HA product as one that will reduce the risk of allergies. The company's website in China currently advises pregnant women to take steps to reduce their baby's allergy risk, including using partially hydrolysed formula when the baby is born. In 2021 the company teamed up with JD Health, China's largest online healthcare platform, to provide information on formula and allergies through JD's app, with content also provided by Chinese and overseas paediatricians.

Nestlé's press release for the initiative cites the German Infant Nutritional Intervention (GINI) study, which it says "confirmed that partially hydrolyzed whey protein formula not only reduces the risk of atopic dermatitis, but also has a protective effect on adolescent asthma." Boyle tells *The BMJ* that the key problem with the GINI study, which he analysed in his 2016 review, was that it selectively reported favourable datapoints. In June 2021 the European Food Standards Agency rejected Nestlé's evidence from the GINI study because of methodological limitations. The agency was also uncertain about whether the formula investigated in the study was the same as the formula under evaluation.

On World Allergy Day 2019, senior Nestlé executives and the chief executive of the popular Chinese parenting website Babytree held an event to promote Nestlé's NAN HA "super energy" hypoallergenic formula. A Nestlé press release said that the "sensitive experience pavilion" taught parents how to prevent their child developing allergies and about the hydrolysis process. While the product pictured in the pavilion was NAN HA 3—a follow-on milk for children aged 12 months and over—research cited in the pavilion and in the press release referred to children aged 0 to 3.

In the same year, Babytree asked mothers to talk about using Nestlé's partially hydrolysed formula in exchange for prizes. Mothers talked about how the formula apparently treated their babies' allergies and eczema.

Nestlé said, "Allergy is a major concern for parents. Our aim is to use our research and innovation to provide them with infant formulas that can help prevent and manage allergies in babies. The efficacy of our partially hydrolysed infant formula in safely reducing the risk of atopic dermatitis is supported by more than 25 strong, independently run and peer reviewed studies. Furthermore, it has been on the global market for over 30 years and approved for use by the EU Commission."

The company added, "We acknowledge EFSA's [the European Food Standards Agency's] opinion that, based on the evidence provided, no conclusion could be drawn on the efficacy of our product in reducing the risk of developing atopic dermatitis. This opinion does not reflect the GINI 20 year follow-up results, which were published following the submission of the dossier of evidence. These results further strengthen the evidence of efficacy of our partially hydrolysed infant formula."

Boyle believes that the GINI 20 year assessment study suffers from similar issues of selective reporting to the other GINI study reports. "There is no trial registration, publicly available protocol, or statistical analysis plan describing the investigator plans," he says. "In the 20 year report, the investigators describe evaluating atopic dermatitis by asking about symptoms, about treatment received, and about a doctor diagnosis of atopic dermatitis—yet they only report outcomes for doctor diagnosis, and we are left without information about self-reported atopic dermatitis symptoms or need for atopic dermatitis treatment.

"So, at least three atopic dermatitis outcomes were recorded, yet only one atopic dermatitis outcome is reported in the manuscript."

Boyle adds that the 25 studies cited by Nestlé as evidence that its partially hydrolysed infant formula reduces the risk of eczema had been reviewed by comprehensive systematic reviews, including by the 2016 *BMJ* publication and by Cochrane. Both reviews found the studies wanting, he says.

Nestlé is far from alone in this. Danone is if anything even more vigorous in its promotion of partially hydrolysed formula for allergy prevention. A video on its Nutriclub.ru page on VK.com, Russia's equivalent of Facebook, advertises the

Box 2 | Brexit—an opportunity for the UK to become a global leader in responsible marketing

In February 2020, new rules came into force in the UK and the EU banning nutrition and health claims about infant formula. The rules are not as strict for follow-on formulas, marketed for babies aged 6 to 12 months, but manufacturers are now required to make a clearer distinction in labelling, presentation, and marketing between these products and infant formulas. These changes initially excluded hydrolysed formula in the UK, but new rules came into force last month.

The rules tighten up the claims that can be made about hydrolysed formula milk. Manufacturers now have to provide evidence that claims about reduced allergy risk have been "scientifically evaluated by an authoritative or scientific body."

Until very recently, Nestlé in the UK was promoting its SMA HA infant milk, a partially hydrolysed formula, which it says can "reduce the risk of developing allergy to cows' milk proteins." But in the run-up to the law change, Nestlé has discontinued the product in the UK market. The National Pharmacy Association has also taken down a Nestlé funded "learning module" for pharmacists that repeated claims that the product could prevent allergy and eczema in children.

For Robert Boyle, clinical reader in paediatric allergy at Imperial College London, Brexit gives the UK the opportunity to "get it right" regarding information provided to consumers about formula products, and he urged for the law to be further upgraded to better reflect the International Code of Marketing of Breastmilk Substitutes.

The code explicitly states that there should be no advertising or other form of promotion to the general public of any breast milk substitutes, including not just infant formula but any milks (or products that could be used to replace milk) specifically marketed for young children up to the age of 3 years.

Victoria Sibson, director of the First Steps Nutrition Trust, says, "The code is an international policy framework for protecting babies, young children, and their parents from marketing practices that commercialise infant feeding, mislead consumers, and threaten breastfeeding. The best way to put a stop to companies' nefarious marketing practices would simply be to adopt 'the code' law, and Brexit affords the UK an opportunity to do this."

Current UK regulation contains all sorts of loopholes that allow spurious nutritional claims to be made. These loopholes include the requirement for statements of intended use on formulas marketed as foods for special medical purposes (FSMPs), toddler milks, and follow-on formulas.

Of particular concern to Boyle is the marketing of FSMPs. "The science behind these milks is generally very weak," he says. "Some do have an effect, but most claims are spurious—for example, products that claim to help colic and crying but with no evidence that they do that. They are meant to be given under medical supervision but are freely available online and in shops. The stated medical indication on FSMPs becomes another way that companies can effectively make claims for their baby formula products."

infant formula Nutrilon Hypoallergenic 1 with the tagline, "Helps to reduce the risk of allergies and in the development of the immune system." An identical video advertisement appeared on its Facebook page. It also advertises Nutrilon 1 and 2 HA on women's lifestyle websites in Ukraine. Danone's 2018 policy for marketing breast milk substitutes says that it will not advertise or promote infant or follow-on formula for children under 12 months of age in higher risk countries such as Russia and Ukraine.

The International Code on Marketing of Breast Milk Substitutes states that there should be no advertising or any form of promotion to the general public of any breast milk substitutes, including infant formula (box 2). Although the code is meant to protect infants up to the age of 3 years, few countries have fully implemented the code into law, meaning that some form of breast milk substitute advertising to the general public is permitted in most countries, including Russia and China.

In 2019 Danone opened a €240m (£201m) production facility in the Netherlands focused on hydrolysed formula. Danone said, "Our baby formulas are based on peer reviewed, clinical research and are inspired by 40 years of breast milk research. Cow's milk protein allergy is a complex medical condition. Many international guidelines have recommended using partially hydrolysed formula to prevent cow's milk allergy.

Families are vulnerable—they are seeking to do the best for their child but do not have a knowledge base on which to form their judgments
Nigel Rollins

"However, the science and understanding of how to reduce risk of allergies continues to evolve, which is why we continue to conduct research with external partners in this field." Danone said it would comply with any new regulations.

It added, "To protect and promote breastfeeding, we report each year on our progress in implementing our strict, worldwide policy for the marketing of breast milk substitutes, and we welcome feedback on where and how we can continue to improve in implementing that policy."

In Russia and Ukraine, Nutrilon HA stage 1 and stage 2 are designated by local legislation as "food for special medical purposes" and not breast milk substitutes, said Danone. "As such, these products are for patients who have been diagnosed with a medical condition, and are prescribed by a healthcare professional. In this communication, we make clear this information is for parents of children who have been diagnosed of being at risk of allergy," it added, pointing out that this was spelled out in its videos on VK.com.

Nigel Rollins of WHO's Department of Maternal, Newborn, Child and Adolescent Health says that childhood health disorders are commonly used to market products with claims based on weak evidence.

"Families are vulnerable—they are seeking to do the best for their child but do not have a knowledge base on which to form their judgments," he says. "They are easily influenced by marketing that identifies a problem and provides a solution in the form of a product.

"There are many examples where products claim to be improving gut health, or immunity, sleep, or brain development, and the evidence used to support these claims is usually exceptionally poor but presented in a way that is convincing. These are areas that governments should be scrutinising more carefully."

For Victoria Sibson, director of the First Steps Nutrition Trust, only robust research should be used to evidence claims. "Breast milk substitute companies exploit regulatory loopholes to get away with making claims about their products which are not backed up by robust research," she says. "Legal but inappropriate marketing misleads parents and healthcare professionals, who are unable to make informed decisions on which formulas to use, especially in the case of clinical need, whether this is perceived or real."

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