this week

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ALAMY

Coroners warn of clozapine deaths

Two coroners have alerted the health secretary for England to two deaths from side effects of the antipsychotic clozapine and asked what action he intends to take to prevent future deaths.

Matt Hancock received the "regulation 28" letters after the deaths of Julia MacPherson and Tom Jackson, amid concerns that healthcare staff may not be sufficiently aware of the drug's serious side effects. Coroners have a duty to send such letters if information emerges during an inquest that could be used to prevent other people from dying in the future.

MacPherson, who had addiction problems and borderline personality disorder, died aged 54 in May 2016 while being treated by Oxleas NHS Foundation Trust. She was put on a trial of clozapine, which her family claimed had made her "unrecognisable." The coroner wrote to Hancock highlighting the trust's failure to respond to the family's concerns.

Oxleas trust told the *Observer* newspaper that a multidisciplinary process had been put in place that would allow families' concerns to be documented.

Jackson, who was subject to a compulsory mental health order, was 24 when he died in August 2016 as a result of "clozapine toxicity, pneumonia and treatment resistant schizophrenia," according to the coroner's report. He spent more than a year taking clozapine at St George's Hospital in Stafford, where his toxicity levels were insufficiently monitored. The coroner wrote to Hancock, "It appears many staff are not aware of the significance of this medication, particularly when considering potential side-effects and warning signs of deterioration."

Clozapine is an atypical antipsychotic mainly used to treat schizophrenia that fails to respond to other antipsychotics. Rare side effects include agranulocytosis, seizures, myocarditis, and severe, even fatal, constipation.

The drug, which is heavily restricted in other countries, has been implicated in other UK deaths, including those of four men in a psychiatric unit at St Andrew's Hospital in Northampton five years ago. An internal report said staff should "be familiar with the side-effect profile and be alert to the possibility of a deterioration in physical health that may indicate a potentially serious or life-threatening adverse reaction or side effect."

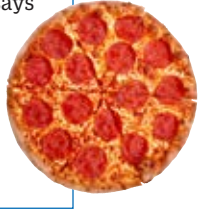
Clare Dyer, *The BMJ*

Cite this as: *BMJ* 2018;363:k5421

The deaths in 2016 of Tom Jackson, pictured at age 7, and Julia MacPherson, when in her 20s, have triggered regulation 28 letters to Matt Hancock, the health secretary

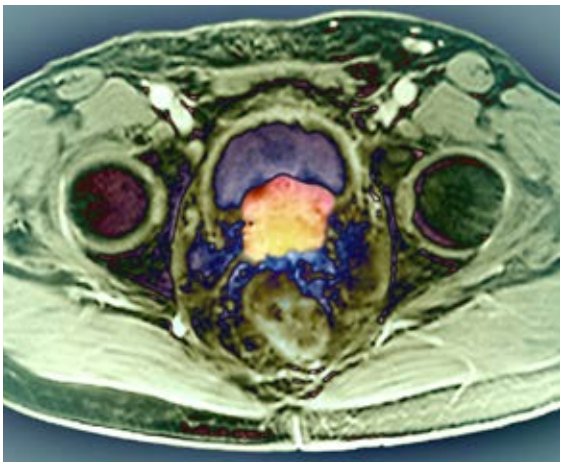
LATEST ONLINE

- More non-EU doctors are taking exams to work in UK, data show
- Locking wards has no place in psychiatric rehabilitation, says royal college
- Tax foods high in sugar and salt to improve nation's health, CMO urges



SEVEN DAYS IN

NICE recommends MRI for suspected prostate cancer to reduce biopsies



Men with suspected prostate cancer should be offered multi-parametric magnetic resonance imaging (mpMRI) to reduce the number of invasive and unnecessary biopsies, says draft guidance from NICE.

Many hospitals offer mpMRI, but a freedom of information request carried out for the charity Prostate Cancer UK earlier this year found that only half of men with suspected prostate cancer were being offered the scan before biopsy. Currently, men are offered a blood test to look for raised concentrations of prostate specific antigen. If these are raised, men may be offered a biopsy, which involves inserting a needle numerous times to sample tissue across the prostate. However, biopsy can miss significant cancer, and it carries a risk of serious infection.

The new draft guidance says that mpMRI scanning should be offered as a first line investigation. This will not replace standard first line tests such as the PSA test, and people who are not going to have radical treatment should not be routinely offered the scan, the guidelines say.

The draft guidelines are out for consultation until 16 January.

Jacqui Wise, London Cite this as: *BMJ* 2018;363:k5290

NHS in England

Safety culture needs radical overhaul

The safety culture of the NHS must transform radically to reduce "never events," the Care Quality Commission warned. Provisional data showed that 468 such events occurred in England from 1 April 2017 to 31 March 2018, including 203 wrong site surgery incidents, 112 foreign bodies retained after surgery, and 35 medicine administration errors. The regulator called for a new training programme to ensure that all NHS staff have a shared understanding of their role in patient safety from the moment they start their first job.

Books balance but local deficits affect care

The NHS in England balanced its books in 2017-18, a review by the parliamentary Public Accounts Committee found, but it warned that many providers had overspent and that local variation can affect patient care. The Department of Health and Social Care spent £120.7bn on running costs and £5.2bn on capital spending in 2017-18, both slight underspends. Providers had overspent, however, with hospitals overspending by £991m and 75 of 207 clinical commissioning groups reporting a deficit. The committee was concerned that local deficits meant that people in some areas experienced worse care than others.

Alternative medicine

Charities must provide evidence of benefit

Organisations that offer complementary and alternative medicine (CAM) and claim that it cures or treats a condition will need to provide evidence of their claims to gain charitable status, the Charity Commission said. David Holdsworth, its registrar and deputy chief executive, said, "Our updated approach means the public will be better able to make informed choices about CAM charities and whether they wish to support them or use their services."

UNAIDS

Head of agency "should be fired"

A damning independent report called for a change of leadership at the UN Joint Programme on HIV/AIDS (UNAIDS) and accused its executive director, Michel Sidibé (below), of creating a patriarchal culture tolerant of sexual harassment, bullying, and abuse of power. It said that the leadership's failure to meet its responsibilities was reflected in repeated examples of favouritism, preferment, and ethical blindness. The agency's programme coordination board agreed to establish a working group to oversee the implementation of the management response to the report. Sidibé said that he would leave as planned in 2019.

Obesity

Control digital marketing to children, says forum

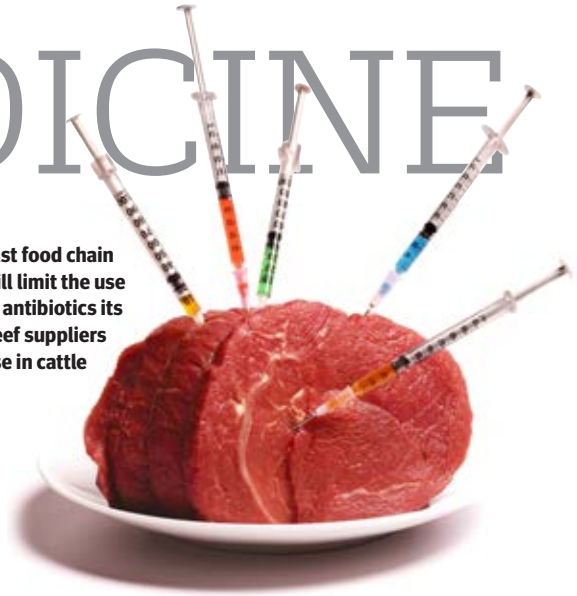
Regulations are needed to control digital marketing directed at children, the World Obesity Federation said, after it found that advertisements in online video games, apps, social media, and other digital platforms are fuelling the obesity crisis. An evidence dossier compiled by the federation found that advertisers used techniques to track children's online behaviour—including their browsing history, location, preferences, "likes," and even emotions—to persuade children to buy food and drink that is high in fat, sugar, and salt.

Breast screening

"Missed" invitations did not exist

An announcement last May by England's former health secretary, Jeremy Hunt, that 135 to 270 patients may have had their lives shortened because they missed breast screening invitations was incorrect, a review concluded. The apparent blunder had been blamed on a computer glitch, but this was found to be wrong. The error has been traced back to 2013, when responsibility for breast screening transferred from NHS England to Public Health England and the new agency thought that screening stopped at age 71, not 70. PHE was too slow to handle the situation, and no one was in overall charge of the screening programme, said the review.

MEDICINE



Fast food chain will limit the use of antibiotics its beef suppliers use in cattle

Antibiotics

McDonalds plans to cut antibiotics in beef herds

The fast food chain McDonalds announced it will cut the use of antibiotics important to human health in the cows that provide its beef, to help slow the spread of antibiotic resistance. The company said that it was working with beef suppliers in 10 countries to set goals by 2020 and begin reporting on reductions by 2022. These countries account for 85% of the beef used by McDonalds in its 37 000 locations.

Overseas news

Pakistani woman seeks sex change to earn living

Kainat Murad, a 22 year old Pakistani woman, petitioned the Peshawar High Court for permission to undergo sex reassignment surgery to enable her to work publicly and support her family. She said that women were not safe at their workplaces and were sexually harassed, humiliated, and exploited. It was her constitutional right to live the life of her choice and change her sex, she said. Khalid Masud, director of the Lady Reading Hospital in Peshawar, told *The BMJ* that the hospital was ready to carry out the surgery if the court sanctioned it.

China "harvested organs on substantial scale"

Forced harvesting of organs from prisoners of conscience in China has been "substantial," said an interim judgment of an independent "people's tribunal" set up to determine if the country's transplantation practices breached international criminal law. The tribunal heard evidence in London on 8-10 December from 30 witnesses including Chinese refugees, doctors, and investigators. Its full judgment, due early next year, could have worldwide implications for doctors and institutions that collaborate with China on transplantations.

Research news

Exercise is as effective as drugs for high BP

Structured exercise achieves modest but consistent reductions in high systolic blood pressure (>140 mm Hg) that are similar to those seen with commonly used antihypertensives, a meta-analysis of randomised trials found. Results reported in the *British Journal of Sports Medicine*

showed that exercise reduced systolic blood pressure by a mean of 8.96 mm Hg in hypertensive patients when they were compared with matched controls.

Removing snacks at checkouts cuts purchases

A UK study showed a 17% cut in purchases of small snacks in supermarkets that removed such products from their checkouts. The results, published in *PLOS Medicine*, showed an immediate reduction in purchases, which was sustained at one year. The study also found a 76% reduction in unhealthy snack foods bought and eaten "on the go" in such supermarkets.

Cite this as: *BMJ* 2018;363:k5398

PARALYSIS

Officials are investigating **28** cases of acute flaccid paralysis reported in England in 2018, most of them since September. Only a few cases are typically seen every year. An increase has also been seen in the US *[Public Health England]*

SIXTY SECONDS ON . . . APPLE ECG

OOH, A NEW APPLE GADGET?
It's a watch, but not as you know it. Apple Watch Series 4 monitors heart rate and can create an ECG from your finger. So you could, in theory, take one when you have chest pain and show it to your doctor later. It can also detect atrial fibrillation.

DOES IT WORK?
At detecting atrial fibrillation, yes. What little data are available suggest it generates more false positives and false negatives than a 12 lead hospital ECG, but not many more.

IS IT "THE ULTIMATE GUARDIAN FOR YOUR HEALTH," AS APPLE HAS CLAIMED?
As the first ECG capable versions arrive in stores, Apple is sounding more circumspect. The app itself is full of warnings that it's no substitute for a doctor. But it could pick up asymptomatic cases of atrial fibrillation, bringing them to a doctor's attention before life threatening events ensue.

BUT REAL ECGs WOULD CATCH THEM?
Indeed. But screening has been deemed pointless. Only a minority of cases of atrial fibrillation are asymptomatic. The US Preventive Services Task Force has given a D recommendation for screening of asymptomatic adults—not even for adults over 65.

TOO MANY FALSE POSITIVES?
You're way ahead of me. And that's with the precision of a hospital ECG. There's also no evidence of survival benefit. What's more, those studies looked at a population of everyday flabby folk. Finding atrial fibrillation among the twentysomething go-getters who buy Apple watches would be like finding a needle in a haystack.

ARE YOU SAYING APPLE CUSTOMERS ARE ALL ATHLETES?
To judge from Apple's marketing, its customers are mostly triathletes. Although the evidence around me suggests that the sofa is a more usual setting for Apple related activity.

SO NOT THE ULTIMATE HEALTH GUARDIAN, THEN?
I can't say. At the September launch, Apple was asked if it felt its products had done more to help or harm people's fitness and cardiac health. The company chose not to answer.

Owen Dyer, Montreal

Cite this as: *BMJ* 2018;363:k5364

NHS trusts struggle to produce Brexit plans amid continuing uncertainty

EXCLUSIVE A lack of concrete guidance from the government is making it difficult for local managers to move beyond basic planning for when the UK leaves the EU, **Gareth Iacobucci** finds

Health secretary Matt Hancock: Announced full no-deal planning on 17 December

LSHTM's Martin McKee: Trusts will be unprepared

Trusts across the UK are finding it difficult to produce contingency plans for Brexit because of the continuing uncertainty about the country's future relations with the EU, an investigation by *The BMJ* has found.

Trusts have been unable to accurately forecast how crucial areas such as supply chains, medicines, and workforce will be affected after the 29 March exit deadline.

The investigation found that only 9% of trusts in England (15 of 161 that responded, out of a total of 231) have established a committee or body to oversee preparations for Brexit. Of the 21 health boards in Wales, Scotland, and Northern Ireland that responded (of a total of 26), 14 have set up a committee.

The BMJ asked all trusts and health boards to disclose any current risk assessment relating to Brexit. Only a quarter of those that responded (47 of 181) were able to disclose this information, and several said they were still assessing the risk. Those assessments that have been done are largely thin on detail, and often trusts assessed similar risks differently.

The investigation shows that trusts are still having problems forging plans for Brexit, four months after the news website Politico reported data from 38 UK hospitals showing that most had not made any formal contingency planning for a "no deal" Brexit.

NHS Providers' Saffron Cordery: Trusts have done what they can

Government action lacking

Saffron Cordery, deputy chief executive of NHS Providers, the body that represents NHS trusts in England, told *The BMJ*, "All the uncertainty has just exacerbated an already difficult situation. Trusts have planned as far as they can, but so much of this is reliant on central government action."

Although the immigration white paper was published on 19 December, she said that this could have been done much earlier "regardless of whether we had a deal or a no deal Brexit."

> **"All the uncertainty has exacerbated an already difficult situation"**
> Saffron Cordery

Because the paper is out for consultation there are still many unanswered questions about who would be allowed to work in the UK after Brexit.

The Department of Health and Social Care for England is overseeing central coordination of risk areas such as drugs, food, medical devices, and clinical consumables. Its position is that trusts are responsible for their own contingency activity, although it is not mandatory for trusts to have a Brexit committee. On 17 December the health secretary, Matt Hancock, told the BBC's *Newsnight* programme that the NHS and health department had instituted "full no-deal planning," but no further specific instructions to trusts were issued.

Plans remain basic

In November Hancock sought to reassure MPs that NHS supplies, workforce, and medicines regulation would be secure in the event of no deal "if everybody does everything they need to do." But with the terms of Brexit still uncertain, much of the detail of what trusts actually "need to do" is not clear.

Responses to freedom of information requests from *The BMJ* show that trusts have drawn up lists of contracts that could be affected by a no deal Brexit, as requested by the health department in October. But most have been unable to move beyond basic scenario planning. For example, some trusts and health boards are taking action to support their staff from other EU countries, including paying for them to gain settled status. Northern Lincolnshire and Goole NHS Foundation Trust estimated that this would cost it about £14 000.

Others have told staff not to stockpile drugs or write longer prescriptions in the weeks leading up to Brexit, as requested by the government.

But it's clear that some trusts are nervous about the future. Royal United Hospitals Bath NHS Foundation Trust, which has a Brexit committee, said that it would advise doctors not to overprescribe but added that some products, such as furosemide and EpiPens, were "already in short supply."

England's largest trust, Barts Health in London, rated its financial plans and sustainability as being at "high risk" because of the lack of "specific plans and contingencies" for Brexit. Delivering its recruitment and retention objectives was also at high risk, it said.

Cordery urged the government to distribute a clearer set of "centralised assumptions" about possible Brexit scenarios to help trusts plan more

THE INVESTIGATION

The BMJ sent freedom of information requests to all 231 trusts in England (including acute care, community, mental health, and ambulance trusts) and the 26 health boards in Scotland, Wales, and Northern Ireland. It received 182 responses (71% response rate): 161 from NHS trusts in England and 21 from health boards.

People's Vote activists protest in August last year about the possible effects on healthcare of a no-deal Brexit

DAN KITWOOD/GETTY IMAGES

Only 9% of trusts in England (15 of 161 that responded) have established a committee or body to oversee preparations for Brexit

robustly. "They need to do it pretty swiftly because the clock is ticking," she said. "Fundamentally the issue is that not enough decisions are being made [nationally], and when they are being made trusts don't really have enough lead time to push them through.

"It would also be easier for us to understand trusts' state of readiness if there were a shared set of centralised assumptions. When one trust assumes they won't have drugs for 12 weeks, and another assumes they won't have them for six weeks, we're not going to be clear about how ready people are."

Cordery cited the fact that the NHS scheme for trusts to help EU workers gain settled status in the UK launched only on 29 November and in a limited number of pilot areas. "If they had rolled this out six to 12 months earlier then that would have been really helpful. I know they're complex to implement, but it's even more complex when trusts don't know what's happening and they can't support their staff," she said.

Extreme concerns

Commenting on the investigation's results, Martin McKee, professor of European public health at the London School of Hygiene and Tropical Medicine, who has written on Brexit for *The BMJ*, said, "The picture painted by these responses is extremely concerning. It is clear that any form of Brexit will have profound implications for the NHS.

"Even though ministers have been unable to provide reassurance that patients will not die as a result of their policies, they have been unable to offer any useful guidance for trusts. It is inconceivable that the NHS will be prepared for anything other than a situation that, in effect, continues the current arrangements by the end of March 2019."

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2018;363:k5346

RESPONSES TO THE BMJ'S INVESTIGATION

East and North Hertfordshire NHS Trust—The "absence of a clear deal in place between UK and EU post 29 March 2019" was one of the main obstacles to mitigating the high risk it would be adversely affected by Brexit, the trust said.

NHS Lanarkshire Health Board—"There is a risk that [we] will not be in full operational readiness for EU withdrawal, especially in areas where there is limited detail regarding change and impact over the workforce and a range of broader product, access and legislation issues with the potential to adversely disrupt continuity of delivery of healthcare services."

NHS Orkney—"It was difficult to make decisions based on information, as nothing was tangible at the moment."

"The reality is that no matter the preparation put in place we will not be able to mitigate against all the problems that Brexit will bring"

Scottish government—"We're working with Scottish health boards to mitigate as much as is possible against the risks that come from any form of Brexit. The reality is that no matter the preparation that is put in place we will not be able to mitigate against all the real problems that Brexit will bring. We have made repeated representations to the UK government on these matters, not least on seeking clarity from them of the potential impact on the supply of medicines." The Scottish government issued guidance setting out Brexit's damaging implications for health and social care, which may have set the tone for local planning.

Immigration white paper: what will it mean for the NHS?

The Home Office's long delayed paper, published just before Christmas, sets out proposed new rules after Brexit

What are the key changes?
The end of free movement between the UK and EU countries and the removal of any preferential treatment for EU citizens over immigrants from other countries. A new single system for skilled migrants from outside and inside the EU will be introduced, with priority given to higher skilled EU workers.

Are there any other details?
The government has accepted the Migration Advisory Committee's recommendation to scrap the annual cap on the number of "tier 2" visas issued to high skilled workers with a UK job offer. Ministers abolished the cap for doctors and nurses earlier this year. The government has "partially accepted" the committee's recommendation to set a £30 000 minimum earnings threshold for skilled EU migrants, subject to further consultations. This threshold already applies to non-EU workers.

How have healthcare leaders responded?
The abolition of the visa cap has been welcomed, but the possible extension of the £30 000 threshold has raised much disquiet. NHS Providers said it was "deeply concerned" about its effect, as starting salaries for nurses, junior doctors, paramedics, midwives, and healthcare assistants fall below the threshold. The BMA's chair of council, Chaand Nagpaul (below), said an arbitrary threshold could be "potentially devastating to patient care and the wider health and social care sector."

Does the government plan to mitigate this?
The white paper states that low skilled workers may be able to apply for short term visas of up to a year. But the Cavendish Coalition, a UK-wide group of social care and health bodies, called for a change to the threshold to ensure the service could be "properly staffed by the skilled care staff it needs."

What is the timeframe?
The government expects to phase in the changes from 2021. It pledged to consider wider evidence of economic effects and pay levels before confirming the future salary threshold.

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2018;363:k5422

DAVID OLIVER, p 23

Breast implants linked to rare cancer are recalled

REX/SHUTTERSTOCK

One of the world's best selling types of silicone breast implants, which have been linked to a rare form of atypical lymphoma (BIA-ALCL), have been removed from the market across Europe.

The recall of Allergan textured implants came after the French agency for the safety of medicines and health products (ANSM) said it was suspending the Conformité Européene (CE) mark for Allergan's Microcell and Biocell products. It means that, for now, the implants cannot be manufactured or sold in Europe, and those held at clinics are being recalled.

French authorities said they had not "identified any immediate risk for the health of women carrying the implants concerned," and the statement did not mention BIA-ALCL.

A global investigation led by the International Consortium of Investigative

Personal situation adds six months to Bawa-Garba's suspension

The Medical Practitioners Tribunal Service has suspended Hadiza Bawa-Garba for a further six months after she told the GMC that personal circumstances meant she needed more time to face a public review hearing.

The trainee paediatrician's case sparked an outcry among doctors over how the GMC exercised its powers, leading to a decision by the government to strip it of its power of appeal.

Bawa-Garba was convicted of gross negligence manslaughter in 2015 after the death of 6 year old Jack Adcock and suspended from the medical register for 12 months in 2017. The GMC appealed the suspension at the High Court, which ruled to strike her off in January 2018.

But doctors raised more than £350 000 to take her case to the Court of Appeal, which in August—taking account of multiple systemic failures—reinstated her suspension.

For a review hearing before the end of her suspension Bawa-Garba would be expected to provide evidence of insight and up to date medical knowledge, along with current references and testimonials.

Written evidence

The further suspension on 19 December followed a review "on the papers"—without a hearing—by tribunal chair, Stephen Killen, a process that can be used when both the GMC

Journalists—involving *The BMJ*—into medical implants found that not all manufacturers had completed adequate safety tests and that technical files needed to get a CE mark were incomplete.

Last month, ANSM advised surgeons to stop using textured breast implants until it took further evidence in February 2019. According to the British Association of Aesthetic Plastic Surgeons, not all textured surfaces are manufactured in the same way and they appear to convey different levels of risk.

Investigation

In the UK it is thought the risk of BIA-ALCL is 1 in 24 000 breast implants sold. The ICIJ investigation found that figures are not more precise because breast implant registries logging procedures have not been comprehensively used. Data from international studies have found, however, that the risk is highest for more robustly textured or polyurethane covered implants and the range is between 1 in 1000 to 1 in 10 000 implants.

The Medicines and Healthcare Products Regulatory Agency told *The BMJ* that Allergan is working with its notified body GMED, based in France, to resolve the matter. In the interim, it has stopped selling textured breast implants and tissue expanders and intend to withdraw any remaining supplies in European markets. An agency spokesperson said, "There is currently no evidence of an increased risk to patients and there is no need for people who have Allergan breast implants to get them removed or have any additional clinical follow-up. We are monitoring the situation closely and will provide updates as necessary."

In a statement, Allergan said the CE mark had been suspended because "the routine review and renewal of our file has not been completed."

It added, "Allergan stands behind the benefit-risk profile of our breast implant products. The ANSM request, and any action, is not based on any new scientific evidence regarding these products. Furthermore, ANSM has not identified any immediate risk to the health of women with textured breast implants."

Deborah Cohen, London

Cite this as: *BMJ* 2018;363:k5401

IN THE UK it is thought the risk of BIA-ALCL is **1 in 24 000** breast implants sold

and the doctor agree on the proposed outcome. Both parties provided written evidence and submissions in advance.

Killen said in his determination, "I have noted that Dr Bawa-Garba has indicated, via her legal representatives, that she feels unable to attend a public hearing at present due to personal circumstances."

A rapid review of gross negligence manslaughter prosecutions, set up in the wake of the case, recommended the GMC lose its right to appeal against tribunal decisions. The government accepted the recommendation, but legislation is expected to take about 18 months.

GMC appeal processes

The review, chaired by Norman Williams, former president of the Royal College of Surgeons, recommended the GMC reconsider its processes to launch an appeal.

MPs on the Health and Social Care Committee suggested the GMC delegate its right of appeal to the Professional Standards Authority (PSA), which has a separate right to appeal. In a letter dated 20 December to Sarah Wollaston, the committee's chair, the GMC said it had taken advice from a leading clinical negligence lawyer that it would be unlawful to impose a moratorium on its appeal powers or to delegate them to the PSA.

GMC is to update its guidance on thresholds to appeal

However, it will be updating its guidance on the thresholds it should apply and on considering context and systemic issues. Appeal decisions will in future be taken by a three person panel, and will be published.

Clare Dyer, *The BMJ*

Cite this as: *BMJ* 2018;363:k5414

FIVE MINUTES WITH . . .

Peter Hotez

The Texan medical college dean tells **Sophie Arie** why he wrote a book defending vaccination

"I became alarmed at the sharp drops in vaccine coverage. Children are now dying because of the 'anti-vax' movement. Most of the children who died in the latest influenza epidemic in the US weren't vaccinated.

"The movement is extremely well organised, with huge funding and bandwidth. There are 480 anti-vaccine websites. Of course, people are challenging their paediatricians because of what they've read. But there is general silence on the pro-vaccine side. The US government has been conspicuously silent. Unicef and the World Health Organization are not recognising the threat this poses to low and middle income countries.

"We have enabled this by refusing to recognise that public engagement is important for scientists. When I was training the message was 'you're not supposed to engage the public.' It was seen as self promotion. But if you are silent you won't achieve your goals. We have to speak up.

"IF YOU ARE SILENT YOU WON'T ACHIEVE YOUR GOALS. WE HAVE TO SPEAK UP"

"I wrote *Vaccines Did Not Cause Rachel's Autism* as a vaccine scientist, a paediatrician, and an autism dad. I've just said, 'vaccines don't cause autism' and here's why. The Institute of Medicine would say something like 'the preponderance of evidence today cannot show any clear link between vaccines and autism.' That sounds to a lay person like hedging.

"I'm hoping it can make as much difference as a book can for parents, for paediatricians who are feeling under siege, and journalists who still frame this as a 'debate' when there is no debate.

"Colleagues are supporting me privately but not speaking out. The anti-vax movement is very aggressive. Who wants to receive an email while standing in line for their morning bagel to find themselves being compared to Hitler?

"We need to give physicians and scientists the tools and training to communicate. It's good some funding grants now demand an advocacy plan. This needs to become part of the way we think."

Peter Hotez is professor and dean of the National School of Tropical Medicine at Baylor College of Medicine, Houston

Sophie Arie, London

Cite this as: *BMJ* 2018;363:k5117

CHRISTMAS 2018 APPEAL

Help the Rohinghya

The charity Doctors of the World brings essential care to refugees who've fled violence in Myanmar for Bangladesh, as **Sophie Arie** reports

This picture of a crying child won at the British Journalism Awards last month for the photographer, Paula Bronstein. When Rohingya refugees first arrived in Bangladesh in September 2017, the priority was to provide food, shelter, and emergency medical aid.

Some 16 months later, more than 700 000 Rohingya men, women, and children have left Myanmar and live in squalid camps. Now, the humanitarian charity Doctors of the World is helping to build the resilience that this population, already traumatised by extreme violence, needs to cope with living indefinitely in crowded, filthy, and unsafe camps.

As part of the global Médecins du Monde network, Doctors of the World delivers more than 350 projects in more than 80 countries through 3000 volunteers. It works worldwide to empower the most vulnerable, and often forgotten, people to access healthcare, and it relies on individual donations to fund its long term care projects.

"The persecution they underwent in Myanmar is still very present in their memory," says Kwihyang Ku, who coordinates Doctors of the World's work in Bangladesh.

"The Rohingya are still deprived of freedom to live in safety and health, to receive a basic education, and to earn a salary.

"Most refugees cannot conceive of a future for themselves or their families, and as conflict continues, their anxiety grows."

But the United Nations has repeatedly stated that conditions in Myanmar are not conducive to returning, and, says Doctors of the World, the refugees fear that the conditions they now live in will become permanent.

"The goal of our teams is to provide primary healthcare but also to take charge of gender based violence and the psychological suffering of this uprooted people," the charity says. Between November 2017 and August 2018, it says it has helped 37 693 people receive healthcare and conducted 2244 mental health and psychosocial support consultations.

The charity also works to raise awareness of mental health problems among the refugees with community outreach sessions.

Sophie Arie, journalist, London sophiearie@fmail.co.uk

Cite this as: *BMJ* 2018;363:k5360

PAULA BRONSTEIN/GETTY IMAGES

EDITORIAL

Government's misplaced prevention agenda

Fixing the health crisis is a choice for politicians, not people

"Prevention is better than cure."[1] It's an old adage, and one the new secretary of state for health and social care, Matt Hancock, chose for his plan to improve healthy life expectancy in the UK, saying: "It's about people choosing to look after themselves better, staying active and stopping smoking ... Making better choices by limiting alcohol, sugar, salt and fat."[2] Public Health England hailed the announcement as "a seminal moment."[3] Others were underwhelmed.[4]

"Most of us are now living longer," states the plan. This is misleading. Decades of increasing life expectancy in the UK have ceased[5]; infant mortality is now rising[6] and life expectancy is declining for many age groups,[7] and for the most deprived groups of women.[8]

Grossly inadequate

Infant mortality is mentioned only once in the new plan: "Stopping smoking before or during pregnancy is the biggest single factor that will reduce infant mortality."[1] Smoking is unquestionably harmful in pregnancy. However, this unreferenced statement is a grossly inadequate solution to rising infant mortality. First, data from NHS digital show 10.8% of mothers in England were smokers at the time of delivery in 2017-18, down from 15.8% in 2006-7.[9] Smoking is decreasing as infant mortality increases.

Second, many other nations are faring better. In the European infant mortality rankings, the UK fell from seventh in 1990 to 19th in 2015.[10] Finally, repeated concerns that the rise in infant mortality

REX/SHUTTERSTOCK

Austerity, poverty, and inequality have greater importance than individual behaviour

reflected worsening socioeconomic conditions[11] were echoed in a recent United Nations report, which says 40% of all UK children are predicted to be living in poverty by 2022.[11]

Government, and especially the secretary of state for health and social care, need to understand that austerity, poverty, and inequality have greater importance than individual behaviour: smoking statistics are improving, and alcohol consumption continues to fall.

Obesity is very unlikely to be the reason why life expectancy has stalled since 2011—the proportion of adults who are obese has been stable since 2010, according to the Health Survey for England.[15] Furthermore, attributing obesity to individual choice ignores the complexity of interlinked political and social factors.

The removal of expert led recommendations from David Cameron's obesity plan is just one example of the power the food industry holds over health policy, as tobacco did (and still does) before it. Attempts to include evidence based interventions, such as limits on advertising to children and junk food promotions, and other industry tariffs, were notably missing from the final obesity policy the government released in 2016,[16] which focused on two things: increasing physical activity and reducing sugar intake.

Individual solutions for society-wide problems

As individual choices are not to blame for worsening UK health outcomes, what is? The recent UN report detailed the groups most affected by austerity—older people, children, women, those living with disabilities, asylum seekers, and migrants.[11] Many of these groups have seen their health outcomes worsen. The evidence is becoming indisputable: austerity is linked to worsening mental health and suicide rates,[17] worse child health outcomes,[18] and higher mortality among older people.[19] So why announce another plan focusing on individual behaviour?

Political leadership

The UN report concludes, "The experience of the United Kingdom, especially since 2010, underscores the conclusion that poverty is a political choice."[11] The current unprecedented worsening in health outcomes—specifically, life expectancy and infant mortality—is also a political choice. Telling individuals to "make better choices" is unlikely to halt the decline. Far greater changes are needed to improve the nation's health, changes requiring political leadership and policies to support social care and healthcare and to narrow widening inequalities.

Experience in other countries shows that major political change can have almost immediate benefits on life expectancy, as seen in East Germany after reunification.[21] The individually focused "prevention plan" is neither new nor seminal and will do nothing to tackle the deepening health crisis in the UK.

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EDITORIAL

Melatonin in children with cancer

Unsupported claims of effectiveness are misleading families

Recent calls have been made for young cancer patients to be given melatonin as part of NHS "standard of care" treatment. The premise is that melatonin "could save lives as well as the NHS money"—by improving survival and reducing adverse side effects.[1] This has generated understandable media interest.[2]

Cancer affects one in 500 children under the age of 14 and is a leading cause of death in childhood. It is highly emotive, with the potential to have devastating effects on the lives of affected families who, quite understandably, will go to extremes to support their children.

Although more than 80% of young people who have cancer diagnosed will survive long term, six out of 10 will experience one or more serious late effects a decade after they completed treatment.[5] Consequently, the search for approaches that increase survival while reducing short and long term morbidity, remains a priority.

Medical and nursing professionals believe there is insufficient evidence to endorse widespread use

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Sleep disorders

Melatonin is an indolamine hormone produced by the pineal gland.[6 7] Its main physiological role seems to be the regulation of circadian rhythms of sleep, with evidence that it is effective in treating sleep disorders, including prevention and management of jetlag.[8] In association with behavioural modification, it is used in the management of sleep disorders in children,[9] including those with learning disabilities and those with disrupted sleep associated with brain tumours.[10]

Melatonin's antioxidant property is the basis for its potential to inhibit the growth of cancer cells, with studies in vitro and in animals suggesting antimitotic or immunomodulatory effects.[9] Melatonin has been tested as an anti-cancer adjunct in clinical trials in patients with many different cancers, though only one trial was in children.

The trials have been drawn together in multiple systematic reviews[10] which often comment on the moderate to high risk of bias in underlying trials as well as their heterogeneity. Such weaknesses make pooled estimates drawn from meta-analysis unreliable and potentially misleading.[11] A clear understanding of the limitations of systematic reviews is essential when interpreting their findings.

One study, not yet published

The only study of melatonin in children with cancer is a preliminary (phase I) dose finding study, intended primarily to identify an appropriate dose for further investigation.[12] This study has been presented as a conference abstract but not yet published in a peer reviewed journal. It showed tolerability, but side effects included nausea, anorexia, dizziness, fatigue, rashes, and weight changes. Notably, children being treated with anthracyclines, a widely used class of anti-cancer drugs in young people, were excluded because of concerns about the possible harmful interaction with such chemotherapy.

The media coverage surrounding the use of melatonin has provoked, in equal measure, interest and concern from families affected by childhood cancer. Many parents have been left wondering if they should give melatonin alongside their child's treatment and are concerned that information about this supplement was not available to them earlier. Medical and nursing professionals in the UK and Ireland believe there is insufficient evidence to endorse widespread use of melatonin by children with cancer at this stage[13] and that claims of effectiveness are misleading to families.

Inadequately supported statements from widely trusted sources may lead families to use melatonin without informing medical professionals. Such statements may cause additional distress to families, who are already under immense pressure. As we strive to offer hope and support to families affected by childhood cancer, all individuals and organisations should exercise responsible caution to avoid unintentionally compounding distress and harm through premature claims of treatment benefits, particularly improved survival.

The evidence for melatonin's use as an anti-cancer agent is currently weak, and in children effectively non-existent. The proposal to introduce melatonin as "standard of care" in young people with cancer is not supportable. Robust evidence from carefully designed and conducted clinical trials must underpin all treatments for cancer in young people, and melatonin is no exception.

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Seven lessons for better patient safety

Healthcare improvement leaders tell **Jacqui Wise** what their countries have learnt in efforts to deliver safer care

This year patient safety leaders from five countries met in Saudi Arabia to share successes and challenges in their efforts to improve patient safety at a health system level. Hosted by *The BMJ*, April's meeting acknowledged a lack of evidence and the need to learn from global exemplars.

"Although healthcare systems differ from country to country," said Fiona Godlee, editor in chief of *The BMJ* and chair of the meeting in Riyadh, "improving patient safety often faces similar obstacles, and we can learn from what has worked and hasn't worked elsewhere."

After the meeting, some participants travelled to Tokyo to join representatives from 44 countries to sign a declaration acknowledging patient safety as vital to universal health, calling for "high level political momentum" to push for safer care.

1. Engage patients

A key message from the Riyadh meeting was that patient engagement is critical to improving safety. Mike Durkin, senior adviser on patient safety policy and leadership at the Institute for Global Health Innovation at Imperial College London, agrees. "Patients can drive the agenda for change—more so than professionals," he says, citing the example of reducing venous thromboembolism in the UK.

Doctors knew that assessing patients for risk and prescribing anticoagulant drugs could help. But only in the late 1990s and early 2000s was there any "real action" to reduce deaths, from a coalition of patient and parliamentary groups. Durkin, who was formerly national director of patient safety at NHS England, told *The BMJ*.

In the Netherlands, patients have had an enormous role in creating momentum for change, says Ian Leistikow, of the Dutch Healthcare Inspectorate, giving the example of complex paediatric surgery. "We now have one centre in the Netherlands because patients wanted change," he said. "Doctors used to say patients don't want to travel—but they do if it means the quality of care is different."

Göran Henriks, chief executive for learning at Qulturum, which develops improvement knowledge in Sweden, adds that involving patients directly in their care can reduce risks. "We have a dialysis process where patients take control and do the whole thing themselves," he told *The BMJ*. "They take the equipment, start the machine, clean the machine afterwards, and so on. As a result, care related infections have disappeared."

Cultural barriers can inhibit patient involvement, warns Don Berwick, president emeritus and senior fellow of the Institute for Healthcare Improvement in Boston, Massachusetts. "Norms of politeness and respect for authority make it harder for people to speak up," he told *The BMJ*. "A just safety culture is one where everyone can speak up all the time. Where they can say what's wrong and can do so without being blamed."

2. Collaboration is key

Another common message among global safety experts is the importance of collaboration, among clinicians, patients, commissioners, and regulators. Leistikow says the Netherlands excels in "collaborative governance"—among healthcare professionals and regulators, citing the country's centralised pancreaticoduodenectomy procedures. The Enhanced Recovery After Surgery Society started the programme, and the Dutch Healthcare Inspectorate implemented it. Switching from low to high volume centres was accompanied by a halving in the mortality rate from these procedures in four years.

Sweden also relies on deep collaboration, with the Swedish Association of Local Authorities and Regions coordinating 20 healthcare systems covering 290 communities. "This has raised the understanding of quality and safety matters," Henriks says. Every year the association evaluates each system for patient safety and publishes the results.

"The science is clear, you can't have safety and secrecy in the same game"
Don Berwick, Institute for Healthcare Improvement

3. A culture of openness

A culture of openness is crucial, the experts agree. "The science is clear," Berwick says, "You can't have safety and secrecy in the same game."

England has the world's largest reporting system, the National Reporting and Learning System, Durkin says, which collects more than two million NHS incident reports a year. An improvement under way is to add the patient perspective of harm into the system. "The idea that staff can report openly and be supported in doing so is paramount to setting the appropriate culture," he says.

Bandar Al Knawy, chief executive of the Ministry of National Guard Health Affair, says of Saudi Arabia: "We have a culture of openness—a no shame, no blame approach." He cites an electronic system for anonymously reporting safety breaches. "We have a management team that look at them almost instantaneously and then create an action plan."

Sweden's Henriks says, "Our indicators and structures for benchmarking are quite strong." But he says quicker response is needed. "A lot of patient safety matters are connected to daily work. It is hard to change daily processes if people get the evaluation six months later."

In 2016 a law came into force in the Netherlands requiring all organisations to have a system to report adverse events to the inspectorate. Leistikow supports this but says providers often write reports for inspectors rather than for employees and the patient. "The process is also too long and too difficult and the quality of the recommendations that come out of it is often not very strong," he says.

Albert Wu, professor of health policy and management at Johns Hopkins School of Public Health in Baltimore, points to problems in the US healthcare system: "Our accountability system, particularly our malpractice system, continues to be broken and creates incentives that are diametrically opposed to openness and the culture necessary. People are afraid to communicate anything because a lawsuit may be pending."

In 2000 Wu wrote in *The BMJ* of the importance of the "second victim" in medical error, recognising the psychological impact on staff. This led to peer support programmes such as the Resilience in Stressful Events scheme at Johns Hopkins, which has been replicated throughout the US and emulated in several other countries.

4. Keep check of checklists

Many fundamental elements of patient safety were first developed in the US—such as root cause analysis, incident reporting, checklists, and surgical time-out procedures—before becoming entrenched in systems worldwide.

"There is a sweet spot. The checklist ideally liberates you from the drudgery of care"
Albert Wu, Johns Hopkins School of Public Health

In the Netherlands, Leistikow says, "At the beginning of the patient safety movement we created a lot of rules. This has worked well and reduced mortality and morbidity." But he warns, "We can't just keep adding double checks to healthcare process because people won't adhere to them if too disruptive for workflow.

"There are far too many rules and regulations—people don't know which ones are important."

Wu agrees to a degree. "There is a sweet spot where you ideally make specific elements routine—perhaps the most boring and the most easily forgotten ones—so that people no longer need to think about them. When they need to, they are free to improvise and be creative, which in some cases is necessary to find a solution. The checklist ideally liberates you from the drudgery of care."

5. Use technology

The roundtable participants noted the vital role that technology plays in improving patient safety, from data collection and surveillance to monitoring and notification.

Al Knawy says, "Digitisation and automation are key drivers of improvements in patient safety." He gives the example of communicating critical imaging results, such as a pneumothorax. "Under our system, once a patient has the imaging done then an email is sent immediately to the physician requesting the result. This creates urgency in care, and this is how technology drives patient safety."

Electronic prescribing is another example of technology advancing safety by removing transcription errors and putting in checks. For example, once it has been noted that a patient is allergic to a drug then systems can automatically prevent its prescription.

Electronic health records should be a good thing, says Wu. But he warns, "In our rush to bring them in we have largely missed an opportunity to improve workflow and efficiency and communication. They have been designed so that they add time, reduce efficiency, and increase frustration—and even this can lead to burn out."

6. Financial incentives

Offering small incentive payments can bring about demonstrable improvements, says Durkin. "It can get a change in behaviour embedded." He says, for example, that 30-40% of patients in England were being risk assessed for venous thromboembolism but within six to nine months of introducing a payment the proportion reached 90-95%.

Wu says, however, it's not always clear that these "pay for performance" interventions actually improve safety. He gives an example of an incentive programme in the US where Medicare will not pay for a procedure if a patient develops a catheter bloodstream infection while in hospital. "It is designed to help keep patients safer but it can just change people's way of documenting things," he warns.

7. Leadership, leadership, leadership

All countries have some way to go to tackle patient safety challenges. The roundtable and summit coincided with the publication of a report from the Organisation for Economic Cooperation and Development, *Flying Blind*, which presented an economic argument for safe, good quality care.[4]

The report stated that 15% of hospital expenditure in wealthy countries is used to correct preventable harm. Up to 25% of patients in primary and ambulatory care settings in rich countries experience harm—often from diagnostic error or delay or from adverse drug events. This rose to 40% in low and middle income countries.

"An important challenge is seeing safety, not as a one-off project this quarter or this year," says Wu, "but building safety more comprehensively into the system."

Berwick concludes, "The three biggest challenges are leadership, leadership, and leadership. A supportive culture, data investment, supporting staff, and a culture of openness all depend on leadership—executives, clinical, boards of trustees, government, and trust leaders."

"Unless leaders take safety seriously and scientifically we won't see systemic progress."

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FEATURE

Has Cochrane lost its way?

Dissent over centralisation culminated in the expulsion of one of Cochrane's founding members. **Melanie Newman** reports on the organisation's internal struggles

"Cochrane needs to become more professional"
Tom Walley, formerly NIHR

"It's understood only leadership speaks for an organisation"
Lisa Bero, ex-board member

The dust has not yet settled on Cochrane, the leading evidence-based medicine group, after it expelled one of its most high profile scientists and founding fathers. Peter Gøtzsche's sacking and the resignation of four board members in protest has been held out by some as a symptom of a wider malaise at the heart of the international network. Cochrane, they say, has lost its way, its members increasingly disenfranchised from a corporate centre focused on income generation and "message control."

Within a decade Cochrane had fundamentally helped to change the way healthcare decisions are made

The Cochrane Collaboration was founded by Iain Chalmers in Oxford in 1993 as a loose knit, international network of 77 researchers to help clinicians and others make informed decisions about drugs, surgery, and other interventions. It aimed to do this through "high-quality, relevant, accessible" systematic reviews of randomised controlled trials. Unpaid scientists would produce the reviews, governed by 10 principles, including open decision-making, and teamwork" and "minimising bias." The questioning of orthodoxies and opposition to centralised control was fundamental to Cochrane's ethos: Chalmers wore a T shirt bearing the words, "Challenge authority." The international collaboration, he said, should be "committed to opposing any tendency for it to become dominated by any nation, institution, or individual."

Peter Gøtzsche's expulsion from the board sparked the resignation of four colleagues and left Cochrane bitterly divided

A quarter of a century later and Cochrane seems to be thriving. Membership is at 12 500 people and growing. Its income has doubled in the past four years to more than £8m. Cochrane centres are opening in Asia and South America. The Cochrane Library boasts 7500 reviews, half of which are accessible without charge (up from 0.05% in 2013 and increasing by 1% a month), with the library free to 3.6 billion people in lower income countries. And more people are using the reviews: they were downloaded 12.5 million times in 2017 (a 28% increase on 2016).

Quantity not quality

But Cochrane's critics contend this growth is not necessarily to be celebrated. "In healthcare, more does not mean better," argues former board member David Hammerstein. "The core business of Cochrane is its systematic reviews, yet in the past decade it has dragged its heels in response to insistent concerns that they are largely synthesised information from industry sponsored studies." He is unimpressed with progress on open access. "After one year of moratorium behind a paywall almost all publications become open access anyway."

Tom Walley, who until recently made decisions on funding Cochrane in his role as a National Institute for Health Research (NIHR) director, agrees the organisation's priorities need to change. "It has become a machine, churning out reviews," he says. The NIHR is partly responsible for this: for years it evaluated Cochrane on how many reviews it produced rather than their impact. "Cochrane needs to be more iconoclastic, more challenging, and more of an advocate for evidence based medicine," he says.

Tellingly, the pair disagree on how these quality improvements are to be achieved. For Hammerstein and many of Gøtzsche's supporters, Cochrane's growing central executive and the tighter control it is exerting on the network's activities, are antithetical to cutting edge science. Hammerstein argues that two opposing views are emerging within Cochrane: that of a collaboration "not afraid of publicly questioning some of the basic social, economic, and scientific premises of our current medical research model" set against a "centralised, functionalist, conformist, and conservative approach." The leadership's centralised approach has isolated it "intellectually and professionally," he maintains.

Walley's view, in contrast, is that more cultural and structural change is required, not less, starting with the review groups, which "were created in the nineties, based on the enthusiasm of people who have now retired." The introduction of networks to set research priorities is a step in the right direction, he says, but do not go far enough. "Cochrane needs to become more professional," he adds.

Internal divisions

While Gøtzsche's sacking is a first for Cochrane, it is not the first time it has been bitterly divided. Its history is punctuated with debates and criticism over conflicts of interest, research quality, and structure.

In the 1990s governance was minimal. Lisa Bero, who has chaired a US Cochrane Centre and sat on the board for more than a decade,

"To be ready for the next 20 years, we need to be transformed"
Mark Wilson, chief executive

COCHRANE'S STRUCTURE

Cochrane is made up of several entities. There are 52 Cochrane review groups (CRGs) incorporated into 8 networks; 17 methods groups; 11 thematic fields; and 20 centres, with 34 associate centres and affiliates in 44 countries.

CRGs conduct systematic reviews within areas set and prioritised by the networks, with the other entities, such as the Cochrane centres, supporting the review group.

Despite Wilson's efforts to expand the numbers of centres—five opened in 2017—some members have questioned the leadership's commitment to their survival. Wilson scotches any suggestion they will disappear.

"The role of Cochrane centres is fundamentally to be the representatives of Cochrane in that geographical space and to drive Cochrane evidence into policy and practice in that country or region—we can't do that from London," he says.

recalls the way the steering committee operated then. "Somebody would say, 'This person is doing some good research, let's give him about £100 000,' and it would be agreed."

Industry influence, however, was taken seriously. Reviewers were asked to consider the harms of interventions on patients, and some members pushed to include unpublished data in reviews. Cochrane's more radical fringes campaigned for access to raw trial data and clinical study reports, looking for evidence beyond industry funded trials and analysis.

Within a decade the organisation had fundamentally helped to change the way healthcare decisions are made. Cochrane's methods drove a collective, international, move towards evidence based decision making. That is not to say its work was infallible. A 1998 assessment of 53 reviews found "major problems" in 29%, with all the problematic conclusions giving too favourable a picture of the experimental intervention.

Despite Cochrane's strong position on industry relations, divisions emerged early on over its conflicts of interest policy. By its 10th birthday the collaboration was at a crossroads over drug company sponsorship. Cochrane's rulebook stipulated that "direct funding from a single source with a vested interest in the results of the review is not acceptable." Yet, *The BMJ* reported the Cochrane library contained two reviews of drugs funded by their manufacturers. The company had agreed to make all data available, so Cochrane decided to waive the rule.

Gøtzsche, director of the Nordic Cochrane Centre, was one of the strongest opponents of the waiver. A former industry insider whose academic career has focused on bias in clinical trials, Gøtzsche proposed a prohibition on industry sponsored reviews at 2003's Cochrane Colloquium, an annual open conference. After lengthy debate Cochrane agreed a policy banning funding of reviews by "commercial sources with financial interests in the conclusions". However, no consensus was reached on funding of centres, and employees of manufacturers were allowed to write and propose reviews.

Success stories

Cochrane's 10th birthday occurred in the year that saw the return of amodiaquine to the World Health Organization's essential drugs list for the treatment of malaria—illustrating Cochrane's growing influence on global health policy. The drug had been banned after case reports of side effects but was reintroduced when a Cochrane review, including unpublished reports, showed it was as safe and more effective than WHO approved chloroquine.

As the decade progressed Cochrane continued to live up to its aim to be "the most reliable source of evidence healthcare." Tom Jefferson and colleagues' finding in 2009 that the anti-flu drug oseltamivir (Tamiflu) offered no clear advantage over aspirin, overturning the findings of his own earlier review, sealed this status. WHO had recommended oseltamivir in response to fears of a flu pandemic, leading many countries to stockpile it.

Cochrane's reputation prevailed against a background of methodological debate and a steady but low key flow of criticism about the quality of reviews, the reviews' sometimes esoteric nature, the time it took to produce and update them, and continued debate over reviewer and trial conflicts of interest. But despite its growth during this decade, the collaboration largely retained its values and organising structure: that of a grassroots organisation, led from the bottom up.

The antimalarial drug, amodiaquine, was reinstated by WHO when Cochrane evidence showed it was safe and effective

Evidence provided by Tom Jefferson's team on Tamiflu changed WHO policy

Corporatisation

That was to change. A strategic review was carried out in 2009 which made 26 recommendations, including an increase in central support for the expanding organisation.

In November 2012, a new chief executive was appointed: Mark Wilson, a former journalist who had worked at the International Federation of the Red Cross but had no clinical or science background. His first task was to turn the recommendations into strategy. "We are a vast organisation, still being managed in an ad hoc ,hand-to-mouth sort of way. To be ready for the next 20 years, we need to be transformed," he said at the time. The strategy was deeply unpopular in some quarters.

"There was challenge from some of the people who are shouting now," Wilson says. He describes his plan, which the board approved unanimously, as "laser-like focused" on review production and on ensuring Cochrane evidence was used in policy and practice. One strand of the strategy was greater unity of brand and message. In 2015 the Cochrane Collaboration was renamed Cochrane.

A new "spokesperson policy" was also issued, prompted in part by concerns about Gøtzsche, who had published a book in 2014 that described the pharma industry as "organised crime," and a *Lancet* paper arguing that antidepressants can cause more harm than good. In the same year a fresh Cochrane review of oseltamivir including hitherto unseen industry

data had confirmed the 2009 finding. These data, whose volume far eclipsed that in the public domain, had been released as a result of a five year campaign by *The BMJ* and Cochrane members, prompting accusations of industry cover-up. In this environment many viewed Gøtzsche as a champion of truth and research quality.

Response to "spokesperson policy" was also mixed. Bero saw the policy as uncontroversial. "I am used to working at organisations where it is understood that only the leadership speaks on behalf of the organisation," she said. "When individuals hide their own views behind an organisation's name, it exposes it to liabilities."

But at Cochrane's 2015 annual meeting the spokesperson policy was questioned by Carl Heneghan, one of the authors of the final review on oseltamivir. When discussing the review with the media he described himself as part of the Cochrane Collaboration. He would not now do so, he told the meeting, and said he was "confused as to whether Cochrane was still a collaboration."

In 2016, centre directors were told they were directly answerable to the chief executive and new "collaboration agreements" were drawn up. Review groups were later organised into eight networks. The aim was to improve the quality of reviews, Wilson says. "

The strategy was not universally welcomed, nor was its implementation. "Are all of the 52 coordinating editors happy that their powers to decide what review to do, when and how they work is being lessened and they're being encouraged and indeed made to work more collaboratively together?" asks Wilson. "No. You wouldn't expect them to be, especially as some have been doing their own thing for 20 years and regard change as an impertinence."

By the end of 2016 Cochrane's income had grown to £6.8m, up from £4.4m in 2014—mainly from review royalties. Staff costs have also more than doubled to over £3m. For many institutions an income rise would be a source of pride, but within Cochrane, resentment at the share taken by the central executive in London—which had not directly earned it—was rising, with frustration at the slowness with which reviews became open access.

For Hammerstein, who joined the board in 2017 the "large expensive London staff" was not only failing to improve research quality but militating against it. High costs mean income must be maintained. "Many long time members are calling for the production of fewer reviews of greater scientific quality, credibility and independence," he says. "But, of course, greatly slowing down the 'systematic review assembly line production' would reduce revenue." At year end 2017, £6.5m of Cochrane's £8.6m income came from review royalties. He says these issues were not discussed sufficiently by the board, which served mainly to "rubber stamp" central executive team decisions.

Board conflicts

Gøtzsche rejoined the board in early 2017 on a platform that made clear his opposition to the direction of travel. He also pushed for stronger action on conflict of interest. At a board meeting in March 2018 Gøtzsche lost an argument for tougher measures to be adopted as soon as possible.

Gøtzsche clashed with the leadership more publicly when a critique, led by him, of Cochrane's review of the HPV vaccine was published. He was also accused by Wilson of breaching the spokesperson policy by using Cochrane's letterhead on a complaint to the European Medicines Agency about its evaluation of possible HPV vaccine harms.

Cochrane instructed lawyers to examine several years of complaints against Gøtzsche. The preliminary legal report submitted in September has not yet been put into the public domain. The same month board members voted six to five with one abstention to expel him—not only from the board but from all his roles. Four of the five who voted for Gøtzsche, including Hammerstein and Gartlehner, walked out.

Documents and statements then released by Gøtzsche and Cochrane stoked the flames of controversy. For an organisation so concerned with messaging the result was not positive. The Iberoamerican group called for an independent inquiry and the Independent Society of Drug Bulletins for the dissolution of the board. Gartlehner says: "The issues have become much larger than Gøtzsche. It's now also about how Cochrane has handled the crisis." He believes a new board would best overcome the rift.

Signatories to Jos Verbeek's petition included some of Cochrane's most loyal foot soldiers

The affair became a lightning rod for discontent from many quarters: opposition to conflicts of influence, improvements in research quality, open access, and outspoken advocacy in relation to all three. After news emerged that Gøtzsche's hospital job was under threat, 8000 people signed a petition to the Danish health minister against his dismissal. Members, led by Jos Verbeek, the work review group coordinating editor, set up a petition asking for action in four areas: open discussion without recriminations; more financial support for review productiont; more member involvement in governance; and increased open access to reviews. This petition secured around 600 signatures—not all members.

Where next?

Grimshaw, who believes Gøtzsche could have "avoided" expulsion, says Cochrane now needs to "establish better working relationships." "It's a wake-up call," he says. "It needs to listen and respond to concerns."

To date leadership has shown little sign of listening. The board has resisted calls for it to resign. Co-chair Martin Burton insists that the majority of Cochrane supported the decision to expel Gøtzsche. "The anti-group has been very vocal, but this is a community of 13 000 people and way over 90% of those people want to move on with the job in hand," he says.

To critics Gøtzsche's expulsion represents the latest step on a path away from Cochrane's founding principles. To its supporters it is a blip in its maturation into a more powerful force. The debate seems unlikely to be resolved easily. Signatories to Verbeek's petition include some of Cochrane's most loyal foot soldiers. These are not employees, who can be forced to toe the line. Retaining the enthusiasm of the volunteer cadre will need more than guidelines. It will require diplomacy, a willingness to admit fault, and good communication—the absence of which arguably caused the crisis in the first place.

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