this week

EMMA BROWN/BMA

GPs threaten mass resignation

GPs have threatened mass resignations from NHS contracts if the government fails to deliver a "rescue package" for general practice.

The BMA's General Practitioners Committee will ask for GPs' views about submitting undated resignations if a bailout plan isn't proposed within six months.

The move was supported by local medical committee (LMC) representatives after a debate at a special BMA conference in London on 30 January.

GPs could also be balloted on the work they would stop doing—to reduce workload and ensure safe and sustainable care—under a motion approved by the conference.

The General Practitioners Committee would also explore actions GPs could undertake without breaching their contracts.

James Murphy, of Buckinghamshire LMC, who proposed the motion, said that the profession needed to take action as hope was "fading fast" for general practice.

He said, "It feels like we are stuck on a permanent warlike footing, lurching from crisis to crisis with only sticking plaster solutions. I feel we are fighting for our very survival." He said that the motion would give BMA negotiators "the arsenal it needs to take on the battles ahead."

Naomi Beer, representing London Tower Hamlets LMC, agreed that the threat to canvass opinion on resignations would force the government and NHS England to take notice.

"We have to get the message through that we will not continue to work within an unsafe system created by others but where we take all the responsibility for failure," she said. "We are at a point where there is nothing to lose because they are killing us anyway. Threatening to resign is not giving up… it is saying we will not be party to this destruction anymore."

Anthony O'Brien, from Devon LMC, spoke against the motion. He warned that canvassing views on resignations would be "pointless" because there was very little chance of securing consensus. "We are here to discuss solutions. Mass unsigned resignations is not one. It won't work, you won't get people to sign up to it," he said.

Chaand Nagpaul, who chairs the General Practitioners Committee, backed the motion. "Let's all collectively do everything we can to safeguard our lives and the care we give to our patients," he said.

Matthew Limb, London

Cite this as: *BMJ* 2016;352:i646

GPs' representatives backed the motion that one doctor said would give BMA negotiators "the arsenal it needs to take on the battles ahead"

NEWS ONLINE

- BMA defends decision to end GPs' responsibility for care home residents
- *Lancet* retracts paper by disgraced Canadian researcher
- General practice is being "eroded" in Scotland, says RCGP

SEVEN DAYS IN

Junior doctors to take strike action next week

Junior doctors will go ahead with industrial action next week as planned, the BMA says, because talks on the new contract have foundered.

BMA negotiators blamed the government's "entrenched position" in refusing to recognise Saturday working as unsocial hours, together with its continued threat to impose a contract on junior doctors that the profession regards as unsafe.

Junior doctors will provide only emergency care from 8 am on Wednesday 10 February to 8 am on Thursday 11 February. Previously, a full walkout with no emergency cover had been threatened from 8 am to 5 pm on 10 February.

Johann Malawana, BMA junior doctors' committee chair, said, "Over the past few weeks, we have welcomed the involvement of Sir David Dalton in talks about a new junior doctor contract which recognises the need to protect patient care and doctors' working lives."

While junior doctors had talked "in good faith" with the government over the past few months they had seen no willingness by the government to move on the core issue, he said, adding, "The government's entrenched position in refusing to recognise Saturday working as unsocial hours, together with its continued threat to impose a contract so fiercely resisted by junior doctors across England, leaves us with no alternative but to continue with industrial action."

Ingrid Torjesen, London Cite this as: *BMJ* 2016;352:i639

Saturday 30th

Proton beam therapy is effective

Proton beam therapy achieves similar survival to conventional photon radiotherapy in children with medulloblastoma and may be less toxic, a prospective study reported. Only 16% of children who had the more targeted proton therapy had significant hearing loss at five years, compared with 24-25% who had photon therapy, and they showed less cognitive deficit. Progression-free survival at five years was 80%, and overall survival was 83%—both similar to the results with conventional radiotherapy. (See *The BMJ*'s full story at doi:10.1136/bmj.i608.)

Sunday 31st

Doctors condemn Hunt's web search advice

The health secretary, Jeremy Hunt, was criticised by doctors for offering "ludicrous" and "potentially fatal advice" to parents who suspect their children of having a rash, the *Independent* newspaper reported. Hunt said that parents who were worried about a child's rash could look at photographs online, as it "may be a quicker way of getting to the bottom of whether this is serious or not." Many doctors took to Twitter, sharing images of rashes and asking social media users whether they could make a diagnosis.

Monday 1st

Gene editing technique is approved for use in human embryos

The Human Fertilisation and Embryology Authority approved a research application from the Francis Crick Institute to use new "gene editing" techniques to slice, repair, or replace genes in human embryos. Researchers at the institute want to study the first seven days of an embryo's development and said that the knowledge gained might be used to improve embryo development after in vitro fertilisation and to provide better clinical treatments for infertility.

Zika virus is public health emergency

The World Health Organization declared the Zika virus a global public health emergency, triggering funding into research, vector control, and efforts to stop pregnant women becoming infected. Margaret Chan, WHO director general, said that growing evidence showed a link between the virus and reported increases in babies with microcephaly and cases of Guillain-Barré syndrome. WHO has not urged any trade or travel restrictions or advised women in countries where the virus is present to avoid getting pregnant. (Full *BMJ* story doi:10.1136/bmj.i657.)

Neurological charities bemoan loss of national clinical director

A decision to abolish the national clinical director for neurology services—the only source of clinical leadership for service improvement in neurology—is "inexplicable" and "short sighted," when 40% of patients wait more than a year for diagnosis and 58% face difficulty accessing specialist services, charities wrote in a letter to the *Times*.

Tuesday 2nd

WHO calls for films with smoking scenes to be rated for age

The World Health Organization

MEDICINE

said that governments should introduce age ratings on films with tobacco scenes and should screen tobacco warnings before the films, to help reduce the number of young people taking up smoking. WHO's *Smoke-Free Movies* report found that films showing the use of tobacco products have enticed millions of young people worldwide to start smoking.

Wednesday 3rd

Mercury in brain is not linked to Alzheimer's neuropathology

Eating seafood once a week or more is associated with higher levels of mercury in the brain, but these were not correlated with more brain neuropathology, a study in *JAMA* found. In fact, the analysis of autopsied brains showed that moderate seafood consumption correlated with less Alzheimer's disease neuropathology. (Full *BMJ* story doi:10.1136/bmj.i611.)

Invitation from GP encourages bowel screening uptake

Almost 40 000 more people might take a bowel cancer test in England each year if the letter inviting them to do so was endorsed by their GP, research published in the *British Journal of Cancer* said. This higher uptake could help to identify as many as 61 extra cases of bowel cancer a year.

Thursday 4th

Cancer death rates fall almost 10% in 10 years

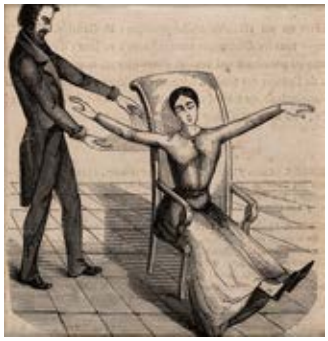
In 2013, 284 in every 100 000 people in the UK died of cancer—10% lower than in 2003, when 312 in 100 000 did so, an analysis by Cancer Research UK showed. Men's death rates fell by 12% and women's by 8% over the 10 years, but death rates from some cancers, including liver and pancreatic, increased.

Smoking ban reaps benefits

The most robust evidence yet, published in the Cochrane Library, showed that national smoking legislation does reduce the harms of passive smoking and that populations benefit from reduced exposure to passive smoke.

Exploring consciousness

This wood engraving of a "mesmerist" practising animal magnetism or "mesmerism"



(now commonly called hypnosis) on a woman features in a new exhibition at the Wellcome Collection called States of Mind: Tracing the Edges of Consciousness. Franz Anton Mesmer, a German physician, formulated the theory that energy could transfer between people and objects, which had a wide following from about 1780 to 1950. The exhibition, which also features a series of changing installations, runs until 16 October.

Cite this as: *BMJ* 2016;352:i659

BOWEL CANCER 40000

more people might take a bowel cancer test in England each year if the letter inviting them to do so was endorsed by their GP

SIXTY SECONDS ON . . . GREENING THE NHS

SO, THE NHS IN ENGLAND HAS HIT A TARGET?

Yes, it has more than met its commitment to reduce greenhouse gas emissions by 10% between 2007 and 2015. Emissions have fallen from 25.7 to 22.8 million tonnes of carbon dioxide equivalent a year—a reduction of 11.3%.

DROP IN THE OCEAN, ISN'T IT?

Yes, given that world emissions amount to nearly 36 000 million tonnes a year. The NHS accounts for about a quarter of the UK public sector's carbon footprint. It's greater than that made by all the passenger aircraft leaving Heathrow Airport added together.

FUNNY, HEALTHCARE NEVER STRUCK ME AS ENERGY INTENSIVE

Two thirds of the emissions are attributable to goods and services that the NHS procures, 19% to direct energy use in buildings, and 16% to travel by patients and staff. The biggest reductions have come from procurement (16%), thanks in part to drug companies cutting the carbon intensity of their products. Travel related emissions have fallen by 5% and energy emissions by 4%.

SO, EVERYBODY'S HAPPY?

Not deliriously. If we chose 1997 rather than 2007 as the starting point there would be no reduction at all to celebrate. Since then carbon emissions have risen, only to fall again to roughly where they started. If the NHS continues at the same rate, it will have achieved a 30% reduction by 2050, when the target is 80%.

MUCH TO DO, THEN?

Indeed. And John Gummer, chairman of the committee on climate change, has said that government policy is confused and not focused enough on carbon reductions.

Nigel Hawkes, London

Cite this as: *BMJ* 2016;352:i605

SUE MARTIN/ALAMY

Doctor restores postwar artwork to rightful glory

A sculptural panel rescued from destruction by a consultant anaesthetist at his hospital went on show in central London this week as an important example of postwar public art in Britain.

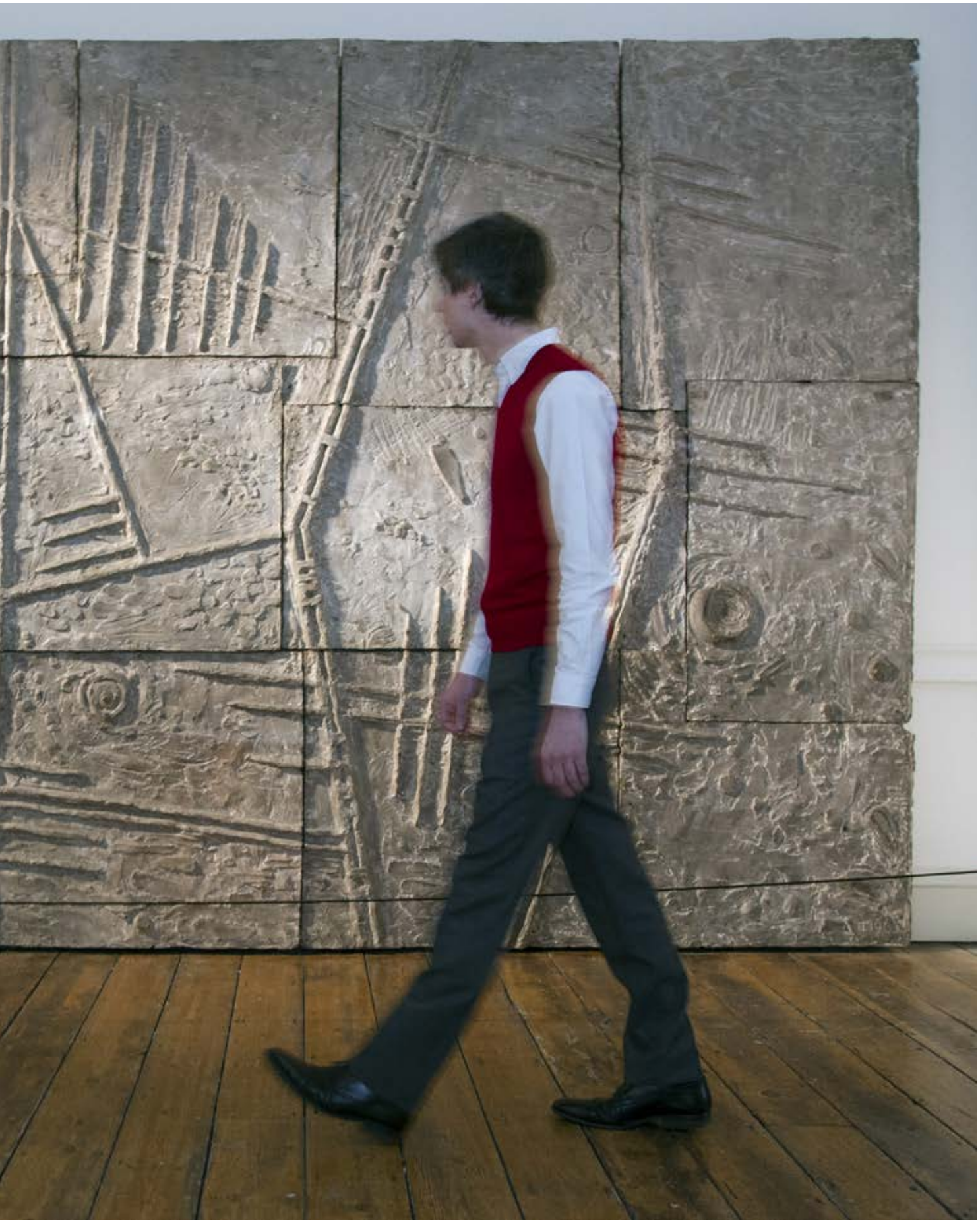
Tim Walker, from East and North Hertfordshire NHS Trust, saved Trevor Tennant's neglected 1963 relief *New Horizons* during a large reorganisation of hospital services last year. At the time the massive concrete and plaster panel, commissioned for Queen Elizabeth II Hospital in Welwyn Garden City, was largely hidden behind a vending machine (below). "I couldn't stand by and see it get destroyed, so I asked if I could have it to buy time to find it a good home," said Walker. "It's not a beautiful work of art, but it is quite striking and of its era."

Tennant was part of a left wing group of artists that produced public art in the belief that creativity should be at the heart of everyday life. The fate of the work after the exhibition, organised by Historic England, closes in April is still uncertain, and Walker hopes it will find a home rather than be sent into storage.

Out There: Our Post-War Public Art is at Somerset House, London, from 3 February to 10 April, £6.50

Rebecca Coombes, *The BMJ*

Cite this as: *BMJ* 2016;352:i672



RICHARD HUBERT SMITH

What doctors think would make NHS 111 safer

Last week England's health secretary, Jeremy Hunt, promised to review the NHS 111 telephone triage helpline, after a report into the death of 1 year old William Mead from septicaemia in 2014. *The BMJ* asked doctors and healthcare leaders for their thoughts on the future of the helpline.

The best triage outcomes occur when the most senior clinicians available undertake it
Peter Holden

MAUREEN BAKER

chair, Royal College of General Practitioners

"Sepsis is very difficult to diagnose. The recent national report on sepsis recommended all GP practices to establish early warning scoring systems to help identify sepsis as early as possible. We look to government to provide general practice with the support and resources to do this in the best interests of our patients."

MARK SPENCER

GP and co-chair, New NHS Alliance (represents care providers outside hospitals)

"One of the main issues with NHS 111 is that non-clinical call handlers don't always have direct access to clinical support. No matter how advanced computer algorithms become, there is no substitute for being able to speak directly to an experienced clinician."

FAY WILSON

GP and medical director of Badger Group (out-of-hours provider)

"NHS 111 is a political talisman which, like NHS Direct before it, seems sacred to all parties. The only consistently useful thing about these services is the single number. If the resources had been made available to GP led out-of-hours services instead, the urgent primary care landscape would have been completely different."

QUESTIONS YOUR PATIENTS MAY HAVE ABOUT ZIKA VIRUS

WHO has declared the Zika virus a public health emergency. The agency said that the evidence for a link between the virus and the increase in cases of babies with microcephaly and a spike in cases of Guillain-Barré syndrome was growing. Here is advice you can use to answer questions your patients may have about Zika virus.

1 I'M PREGNANT AND PLAN A HOLIDAY TO GUADELOUPE. SHOULD I GO?

Public Health England and the National Travel Health Network and Centre advise that women who are pregnant (any trimester) or who plan to become pregnant should consider avoiding travel to any area where active transmission of Zika virus is being reported (box). They say that if you can't avoid travelling to one of these countries you should take great care to avoid mosquito bites.

2 WHAT ANTI-MOSQUITO MEASURES SHOULD I USE?

The US Centers for Disease Control advises pregnant women to wear clothing that covers up as much of their body as possible (long sleeves, trousers, hat). It also advises travellers to use a good repellent on exposed skin during the day as well as at night and particularly during mid-morning and late afternoon to dusk, when the mosquito that transmits Zika is most active. Repellents that contain DEET, picaridin, and IR3535 are all safe for pregnant women, provided that they follow the instructions, says the CDC. It says that if you need sunscreen you should apply repellent after sunscreen and you should stay or sleep in a screened or air conditioned room or use a bed net.

Men who have been infected with the Zika virus are advised to use a condom for six months

3 WHAT ARE THE SYMPTOMS OF ZIKA VIRUS INFECTION?

Most people infected with the Zika virus will not get symptoms, and if they do these are usually mild. Symptoms can include fever, rash, itching, joint pain, headache, muscle pain, eye pain, and conjunctivitis. There is no specific treatment, but you can take paracetamol for a fever and to ease any joint pain. If you're pregnant and think

FELIPE DANA/AP/PA

PETER HOLDEN

former lead negotiator for NHS 111 on BMA's General Practitioners Committee

"The tragic case of William Mead is the consequence of 111. NHS 111 is supposed to be a triage tool. The best triage outcomes occur when the most senior clinicians available undertake it, because triage of necessity requires clinical judgment. This is not something that can be codified into a tick box algorithm, because either the system will grossly over-triage and overload other components of the system or will seriously under-triage patients, resulting in disasters."

NEENA MODI

president, Royal College of Paediatrics and Child Health

"The younger the child, the more difficult it is to detect serious illness such as sepsis. The college therefore calls for a well conducted evaluation of the effectiveness of NHS 111 in providing advice about sick children. It also calls for mandatory training in child health for GPs—something that has already received support from governments of all four nations and now requires funding—and easily accessible information for parents."

Gareth Iacobucci The BMJ

Cite this as: *BMJ* 2016;352:i638

you have been infected with the Zika virus you can be tested.

4 I HAVE JUST RETURNED FROM MEXICO. MY WIFE IS PREGNANT. IS IT SAFE TO HAVE SEX?

Most cases of Zika are acquired by mosquito bites, but the virus has been shown to be present in semen. The risk of sexual transmission of Zika is thought to be very low, but Public Health England advises men who have been in a country with Zika virus transmission to use a condom for 28 days. Men who have had an unexplained fever and rash that could have been caused by the Zika virus or have been told that they have Zika infection are advised to use a condom for six months.

5 I'M PREGNANT AND HAVE JUST COME BACK FROM THE CARIBBEAN. I'M WORRIED MY BABY MAY HAVE MICROCEPHALY

The Royal College of Obstetricians and Gynaecologists advises that women who've had no symptoms or whose symptoms have resolved should be referred for ultrasonography, which can be repeated every four weeks. Women with symptoms indicating Zika virus infection should have samples sent to the Rare and Imported Pathogens Laboratory (clotted blood, an EDTA "purple top" blood, and a small volume of urine without preservative). Women who test negative should be referred for ultrasonography, which can be repeated every four weeks. Women who test positive should be referred for ultrasonography and to fetal medicine for follow-up.

For all *The BMJ*'s latest articles on the Zika virus epidemic go to bmj.co/zika.

Zosia Kmietowicz, *The BMJ*

Cite this as: *BMJ* 2016;352:i649

COUNTRIES WITH ACTIVE ZIKA VIRUS TRANSMISSION AS AT 29 JANUARY 2016

- Barbados
- Bolivia
- Brazil
- Cape Verde
- Colombia
- Dominican Republic
- Ecuador
- El Salvador
- French Guiana
- Guadeloupe
- Guatemala
- Guyana
- Haiti
- Honduras
- Martinique
- Mexico
- Nicaragua
- Panama
- Paraguay
- Puerto Rico
- Saint Martin
- Samoa
- Suriname
- US Virgin Islands
- Venezuela

Further cases of Zika virus disease are expected to be reported in other countries where the mosquito vector is present, particularly in the Americas

FIVE MINUTES WITH . . .

Chaand Nagpaul

After a crisis GP summit on 30 January *The BMJ* spoke to the chairman of the BMA's General Practitioners Committee

"The BMA's local medical committees conference was a meeting of local representatives of GPs, many of whom were representing practices that are on the brink of collapse. The meeting drew on these fears of thousands of GPs, and they were relaying the reality on the ground. That reality is clearly not sustainable, and it is affecting the quality and safety of the care we're providing.

"The most immediate thing is that GPs want a manageable and safe workload. They want measures that will, in real terms, reduce workload to manageable limits so that GPs can provide safe quality care on a daily basis. At the moment they believe that they are compromising care and, furthermore, that the excessive workload is damaging their own health.

"To achieve this, firstly there will need to be national and local systems of ensuring that we manage demand. Another element is providing general practice with the resources to enable GPs to have a manageable workload—so that will be new resources. I say this at a time when we don't have enough GPs, so it will require investment in staffing. We need to provide real resources to stabilise general practice, especially where practices cannot survive.

"There is a strong feeling among GPs at this time that there is the additional burden of over-regulation of practices. The impact of Care Quality Commission inspections on practices can't be over-exaggerated: it is a real pressure.

"It would be folly for the government to ignore this resounding message from the conference. Even talk about mass resignation is not so much theory but a reality that the government's own statistics tell them is likely. We've come to a juncture where the government cannot ignore the messages from this conference or the reality. The fact that the secretary of state has talked about an announcement shows that they understand there is a problem. But what we're saying is that understanding there's a problem has to be followed up with real tangible policies and investments to address the core cause of this: neglect and chronic underfunding."

Gareth Iacobucci, *The BMJ* Cite this as: *BMJ* 2016;352:i640

EDITORIAL

Statutory body needed to expose medical fraud

It's increasingly hard to ignore the need for statutory regulation to tackle research misconduct

Anjan Kumar Banerjee, a surgeon, spent the years 2002 to 2008 erased from the medical register for serious professional misconduct related to research fraud, financial misconduct, and substandard care, yet in 2014 he was awarded an MBE "for services to patient safety."[1] This embarrassing mistake was quickly rectified, and the MBE forfeited. But he remains a fellow of three medical colleges. Each either awarded him or reinstated a fellowship after his erasure, and the University of London has not withdrawn his MS degree, which has been known for 15 years to be based on fraudulent data. The long sorry story of Banerjee that cardiologist Peter Wilmshurst tells in the linked analysis article[1] raises serious questions about the integrity of medical and scientific institutions.

Wilmshurst's story comes a few weeks after an article in the *Times Higher Education* about a report to government that says: "Senior figures in UK science have warned that despite decades of awareness of the cultural problems driving misconduct in science, little progress has been made . . . The draft . . . concludes that some research institutes, university administrators, funders, journals and science leaders have been covering up malpractice."[3]

But what the report says is not news. Although Britain has had various initiatives, it has never managed to mount a serious response to research misconduct. Many scientific leaders still do not acknowledge the seriousness of the problem, fooling themselves that research misconduct is rare, science is self correcting, and misconduct is a victimless crime. Universities jealously guard their independence: even though they depend heavily on government funding they don't want government bodies having powers to investigate possible misconduct of their researchers.

But universities clearly have a major conflict of interest when one of their researchers is accused of misconduct. It is tempting to try to bury the whole thing, perhaps encouraging the miscreant to retire early or move on rather than be investigated. Until recently universities and other institutions could be confident that they would get away with burying the case.

Wilmshurst has many other disturbing stories in addition to the Banerjee one; these, as he writes, can often not be told publicly because of the expense and difficulty of getting them through lawyers.[1] *The BMJ* recently published an account of the case of R K Chandra, whose multiple frauds were buried for 20 years by his Canadian university."[10-12] *The BMJ* and other journals belonging to the Committee on Publication Ethics have over the years asked many other research institutions to investigate worries, and often nothing has happened.[13]

There is no shame that misconduct occurs in your institution, but there is disgrace in failing to deal with it properly

Long time rotten

We have no way of knowing how many cases are successfully covered up, but when talking to meetings on research misconduct, I ask how many people know of a case of research misconduct. Usually a half to a third of people put up their hands. I then ask whether the case was fully investigated, and if appropriate the perpetrator punished and the record corrected: hardly any hands remain raised.

So what should be done? We do need to move to a world where universities recognise the rightness of investigating allegations of misconduct and commit to punishing those found guilty and to publishing the results of their investigations, correcting the research record, and retracting fraudulent research. There is no shame that misconduct occurs in your institution, but there is disgrace in failing to deal with it properly. But after years of inaction it's hard to escape the need for a statutory body with powers that can oversee research institutions, including universities.

And what about royal colleges? A fellowship of a college explicitly endorses a doctor's competence and probity so it's shameful that the colleges do not retract Banerjee's fellowships, and their failure to do so raises questions about their competence and integrity.

Something is rotten in the state of British medicine and has been for a long time. Statutory regulation is needed.

Richard Smith, chair of the board of trustees, icddr,b, Bangladesh
richardswsmith@yahoo.co.uk

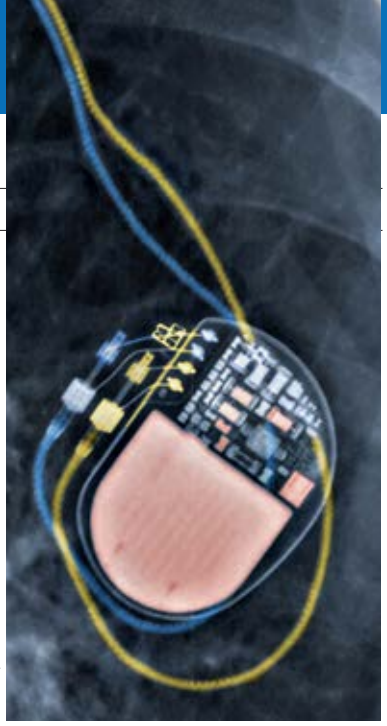
Cite this as: *BMJ* 2016;352:i293
Find this at: http://dx.doi.org/10.1136/bmj.i293

ANALYSIS, p 190

EDITORIAL

Pacemaker battery scandal

Much can and should be done to maximise the longevity of existing devices



APOGEE/SPL

Imagine spending £3000 on a new watch with a battery embedded in the mechanism that cannot be replaced or recharged. Although the battery is predicted to last 10 years or more, after six years you discover that it is running flat and you're advised to replace the watch immediately, even though it may keep good time for a year or more.

This mirrors the dilemma faced by all patients with cardiac implantable electronic devices such as pacemakers and implantable cardioverter defibrillators (ICD). But for them the stakes are much higher as replacing the battery exposes them to a risk of serious complications, including life threatening infection.

Over half of all patients with pacemakers require a replacement procedure because the batteries have reached their expected life.[1] Some 11-16% need multiple replacements.[2] The situation is worse for recipients of an ICD, since the risks of infection at the time of implant and device replacement are higher than with pacemakers and the batteries have a shorter life.[3]

What is the risk of infection?

With no standard definition or reporting system, quoted infection rates vary widely, and the commonly quoted risk of 0.5% for new implants and 1-5% for replacement procedures may be wrong.[4] Infection, even if it seems superficial, usually necessitates extraction of the entire system. Simply treating the infection with antibiotics results in a much poorer outcome.[5] The increased risk of infection associated with battery replacement makes it critical that we prolong the life of implantable devices as much as possible. The health economic grounds for minimising the number of replacements are also compelling.[6]

The current financial model discourages the development of longer life devices. Increasing longevity would reduce profits for manufacturers, implanting physicians, and their institutions. With financial disincentives for both manufacturers and purchasers it is hardly surprising that longer life devices do not exist.

Patients are often assumed to prefer smaller devices, but when offered the choice, over 90% would opt for a larger, longer lasting device over a smaller one that would require more frequent operations to change the battery.[7] And given the risks that patients are exposed to during replacement, there is an urgent need to improve longevity by developing longer life batteries and using those in current devices more prudently.

We need to review the timing of replacement of implantable devices in all patients

What can be done now?

At present the main drive to improving longevity of pacemakers has been through programming changes aimed at reducing the amount of pacing[8] or minimising the drain of current during pacing—for example, using high impedance leads. But devices are usually replaced when there is still substantial life left in the battery. For example, when a pacemaker reaches elective replacement indication, it is usually 3-12 months before it will reach its end of life. And even then, the battery may continue to function for several months. Early replacement may be reasonable for high risk patients (such as those who are entirely dependent on their pacemaker). However, we could delay replacement of the pulse generator until the batteries are virtually depleted in lower risk patients. The increasingly popular innovation of home monitoring of devices would facilitate this.

For ICDs the waste is even more striking; devices reach their elective replacement indication when they are still capable of delivering at least six full energy shocks. Each shock reduces the battery longevity by about 30 days. So for patients who receive no shock therapy we are prematurely discarding a device costing up to £25 000 (€33 000; $36 000), which could last at least another six months (current devices last four to seven years on average). We need to review the timing of replacement of implantable devices in all patients.

STEPS TO MINIMISE REPLACEMENT OF CARDIAC IMPLANTABLE ELECTRONIC DEVICES

- Maximise the longevity of existing devices by:
  - Smart programming
  - Allowing batteries to deplete for longer before replacement
- Invest more in research in rechargeable technology and energy harvesting
- Manufacture pacemakers with a ≥25 year life expectancy so that patients can be offered this choice
- Consider whether device replacement is necessary —every time

What could be done in future?

With existing technology engineers could design and build pacemakers that would last for 25 years or more, with an increase in volume of the device of about 40%. Further developments in battery technology might enable smaller or rechargeable devices.

There is an urgent need to minimise the requirement for replacement of these devices (box). Doing so will save lives, minimise suffering, and reduce costs.

Cite this as: *BMJ* 2016;352:i228

Find this at: http://dx.doi.org/10.1136/bmj.i228

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Neil Sulke, consultant cardiologist, Eastbourne Hospital, Eastbourne, UK

ONLINE HIGHLIGHTS FROM THEBMJ.COM

FROM THE ARCHIVE: THIS WEEK IN 1916

Caesarean section in a pitman's cottage. R Gordon Bell recounts how he successfully performed a caesarean section in the "one clean room" of a pitman's cottage. His patient had been in labour for fifteen hours with no sign of the baby's head engaging in the pelvis. The woman had lost two previous babies in childbirth and she and her husband, a miner at Seaham Colliery, Sunderland, were unwilling to risk the loss of another child. The child, a girl weighing 8 lb, "lacked the usual frontal and occital moulding of the ordinary baby, and therefore looked more like a child a month old."

Bell concludes: "In 1907, at the spring meeting of the Northumberland and Durham Medical Society, I showed a number of major abdominal operations done in private houses, and an interesting discussion took place on the possibility of doing most operations in the homes of patients, and thus relieving the pressure on hospitals."

Cite this as: *BMJ* 1916;1:195

OVERHEARD ON TWITTER

@dr_emmacoombe
Great to see simple overview of diabetes in children and young people in this week's @bmj_latest

@LWiC_QI Interesting
@bmj_latest commentary which looks at how to reduce hospital admissions from care homes: bit.ly/1KeL37p

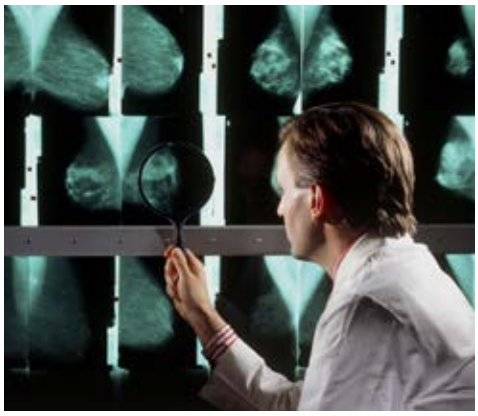
Twitter @bmj_latest

MOST READ ONLINE

When somebody loses weight, where does the fat go?
BMJ 2014;349:g7257

How Jeremy Hunt derailed clinician led progress towards a seven day NHS
BMJ 2016;352:i187

Why cancer screening has never been shown to "save lives"—and what we can do about it
BMJ 2016;352:h6080



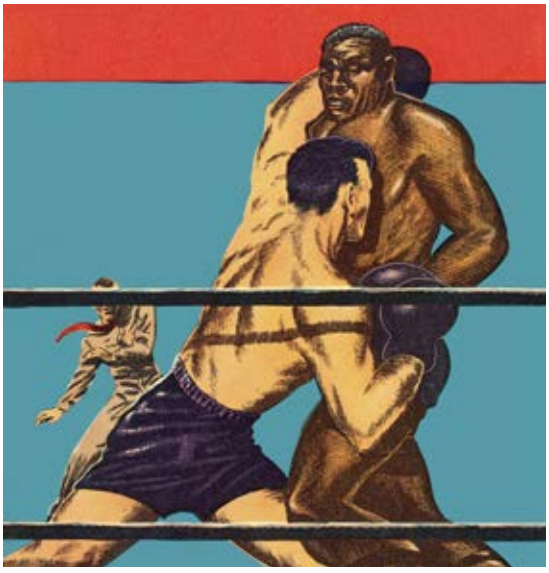
GEOFF TOMPKINSON/SPL

RAPID RESPONSES

Should we ban boxing?

"In comparison [to boxing] football and rugby cause far more fractures and have significant morbidity as well. Should we ban these sports too? Where do we stop?"

Alexander M Wood, orthopaedic surgeon



BLOG OF THE WEEK

The view of a LAT trainee

In January 2016 NHS employers withdrew locum appointed for training posts in England. Paul Sooby, currently undertaking an LAT post, explains why it has been good for his career, training, and morale, and calls for the scrapping of these posts to be reconsidered.

http://blogs.bmj.com/bmj/2016/01/27/paul-sooby-the-last-of-an-endangered-species-the-view-of-a-lat-trainee/

RIVAROXABAN
Can we trust the evidence

An investigation has uncovered the use of a faulty device in the key regulatory drug trial, casting doubt on the results. **Deborah Cohen** reports

Doctors and scientists are calling for an independent investigation into the key trial underpinning use of rivaroxaban to prevent ischaemic stroke in non-valvular atrial fibrillation after *The BMJ* found that a defective point of care device was used in the warfarin arm of the trial.

Doctors and scientists have also told *The BMJ* that the validity of the trial—called ROCKET-AF and published in the *New England Journal of Medicine* in 2011[1]—is in question until such independent analysis is done.

The drug was manufactured by Bayer and marketed in the United States by Janssen, part of Johnson and Johnson, and the companies relied on a single trial–ROCKET-AF—to gain approval from the US and European regulators. The trial included over 14 000 patients and found that rivaroxaban was non-inferior to warfarin for preventing ischaemic stroke or systemic embolism. There was no significant difference between groups in the risk of major bleeding—although intracranial and fatal bleeding occurred less often in the rivaroxaban group.

But there are now concerns about these outcomes. In a letter submitted to the *NEJM* (as yet unpublished) and shown to *The BMJ*, former cardiovascular and renal drug reviewer for the Food and Drug Administration (FDA), Thomas Marcinicak, says: "The care for the warfarin control arm patients [in ROCKET-AF] appears to have been compromised."

Earlier last year, *The BMJ* found that the point of care device used to measure international normalised ratio (INR) in patients taking warfarin in ROCKET-AF had been recalled in December 2014. An FDA class I recall notice (the most serious kind) said that certain INR devices could deliver results that were "clinically significantly lower" than a laboratory method. It added that Alere—the device manufacturer—had received 18 924 reports of malfunctions, including 14 serious injuries. The company confirmed to *The BMJ* that the fault went back to 2002, before the ROCKET-AF trial started.

A falsely low reading could mean that patients had their warfarin dose unnecessarily increased, leading to a greater risk of bleeding. In terms of the trial results, it could make rivaroxaban seem safer than it was in terms of the risk of bleeding and throws doubt on outcomes used to support the use of the world's best selling new oral anticoagulant.[2]

Back in September 2015, *The BMJ* asked the investigators named in the *NEJM* paper about the recall. They included researchers from Bayer, Johnson and Johnson, and the Duke Clinical Research Institute, which carried out the trial on behalf of the drug companies.

None of the authors responded, but a spokesperson for Johnson and Johnson contacted *The BMJ* to say that they were "unaware of this recall" and they took the journal's concerns "seriously." But it took months of probing by *The BMJ* before the companies, world drug regulators, and Duke began to investigate the problem in earnest.

Joining the dots

As for the regulators, when *The BMJ* contacted the European Medicines Agency in April 2015 and subsequently the FDA, both said they did not know that the recalled device had been used in ROCKET-AF. It's new territory for the regulators. What happens to a pivotal drug trial when a device used is found to be defective?

In November the EMA told *The BMJ* it was investigating, and the agency subsequently told journalists: "Due to the defect it is now thought that the INR device may have impacted the clotting results in some patients in the warfarin group."[4]

It would be nice to have some independent study carried out to give confidence in the use of this medicine
Guido Rasi, EMA

Executive director of EMA, Guido Rasi, also called for further independent investigation into direct oral anticoagulants. "It would be nice to have some independent study carried out to give confidence in the use of this medicine," he said.

The FDA also told *The BMJ* that it is "aware of concerns regarding the INR device and its use in the ROCKET-AF trial and is reviewing relevant data." It subsequently announced

DIRECT ORAL ANTICOAGULANTS

Rivaroxaban is a factor Xa inhibitor and belongs to a class of medicines known as the direct oral anticoagulants (DOAC), which also includes dabigatran, apixaban, and edoxaban. They have gained popularity in place of warfarin for the prevention of ischaemic stroke in non-valvular atrial fibrillation because routine blood monitoring is not required.[3]

that it will hold a public workshop about the safety and effectiveness" of point of care INR devices in March "to seek and identify potential solutions" to what it said were "scientific and regulatory challenges."

However, spokespeople for Johnson and Johnson and Bayer issued identical statements in December 2015: "We have conducted a number of sensitivity analyses. These sensitivity analyses confirm the results of the ROCKET-AF study and the positive benefit-risk profile of Xarelto (rivaroxaban) in patients with non valvular atrial fibrillation."

But what should happen amid the uncertainty?

Harlan Krumholz, professor of medicine (cardiology) at Yale University, says that the *NEJM* should place an "immediate expression of concern" on the paper to notify the medical community.

"The study should be considered of uncertain validity until a more thorough review can be done," he says, adding that there should be "an investigation by an independent group of experts to quickly determine if there are grounds for retraction."

The study should be considered of uncertain validity until a more thorough review can be done
Harlan Krumholz

Concerns about warfarin control

Even before rivaroxaban was approved in Europe and the US in 2011 for use in non-valvular atrial fibrillation, regulatory officials raised concerns about the warfarin control in the ROCKET-AF trial. Two primary clinical FDA reviewers of the drug recommended that it should not be approved for the US market.

"ROCKET provides inadequate information to assess the relative safety and efficacy of Xarelto in patients whose warfarin administration can be well-controlled," they wrote in an FDA decisional memo—which outlines clinical reviewers' view on whether a drug should be approved.[5]

However, they were seemingly unaware that there are other reasons to be concerned about the adequacy of the warfarin control in the ROCKET-AF trial that have since emerged.

Lack of transparency over devices in trials

Currently, there is little public information about which diagnostic point of care devices are used in any of the direct oral anticoagulant trials (see box, facing page). They are not named in the published phase III trials. *The BMJ* became aware that the problematic device was used in the ROCKET-AF trial only by reviewing European regulatory documents in April last year.

Marciniak says that the *NEJM*, which published the trials for three of the direct oral anticoagulants, should rectify that.

"You should require that the devices used in trials are clearly and specifically identified in your publications," he wrote in his letter.

How has this come to happen?

In tracking the faulty recall and its potential effect on the outcomes of a global clinical trial, *The BMJ* has once again come across flaws in device regulation. A series of journal investigations have highlighted the lack of clinical data required by regulators for high risk implants, such as metal-on-metal hips, before they are put on the market.[8] They have also shown how slow regulators can be to act when problems do emerge and how oversight can be lacking on the performance diagnostic tests.[9 10]

In 2005, a warning letter from the FDA to HemoSense—the company that marketed the faulty device before Alere bought it—reprimanded them for failing to investigate "clinically significant erroneous" high and low INR results generated by the point of care device.

"Both high and low test [INR] results have the potential to cause or contribute to a death or serious injury, because: they may result in erroneous dosing and thus improper control of coagulation," the letter said.[11]

Despite these warning letters, the FDA cleared subsequent iterations of the device through its 510(k) regulatory system. This system requires makers of such devices to show only that the new version is "substantially equivalent," or similar, to one already on the market. It has been criticised by the likes of the Institute of Medicine for not providing enough evidence that a device is safe and effective.[12]

Johnson and Johnson, however, has lobbied against tightening up this aspect of device regulation and the need to provide more evidence.[13] But the lack of a regulatory requirement for the diagnostic accuracy of the device to be checked before it came on to the market has allowed the fault to creep through the system.

Alere has confirmed to *The BMJ* that the fault dates back to 2002 and it may occur in all devices and not just one batch. However, neither it nor the FDA responded to questions about why nothing had been done about the problem earlier.

Were the companies aware of any problems during the trial?

The BMJ asked Johnson and Johnson, Bayer, and Duke if any investigator complained to them about mismatched point of care and laboratory INR readings if someone had a bleed in the trial. *The BMJ* also asked if they had validated the device at any point before or during the trial. None responded to the questions.

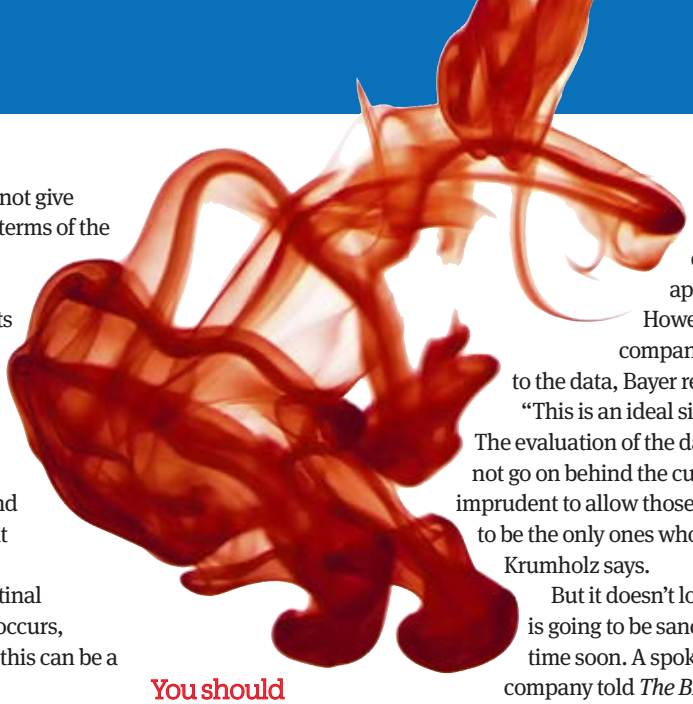
What next?

The EMA has told *The BMJ* that it has asked the companies for analyses and would consider any analyses by Duke too. During the trial INR at 12 and 24 weeks was measured at a central laboratory as well as with the point of care device. Powell says that "a comparison should be made between the defective point of care readings and the two sets of 'gold standard' central lab readings" as this would "determine whether this defective device undermined the integrity of the trial results."

It is not clear that this has happened. In December last year, Duke issued a press release with a summary report of the results of their "secondary analysis of the trial findings."

"The findings from the analysis are consistent with the results from the original trial and do not alter the conclusions of ROCKET-AF—rivaroxaban is a reasonable alternative to warfarin and is non-inferior for the prevention of stroke and systemic embolism with less intracranial hemorrhage and fatal bleeding," it said.

But Powell says this statement is "misleading" because of the lack of information.



Krumholz also thinks that this statement did not give enough information about what Duke found in terms of the major safety endpoint—major bleeds.

"The DCRI is among the most respected research institutions, but this statement suggests that they know important information that relates to the ROCKET-AF trial but are delaying in disseminating the information until it can be published," he says.

Hugo ten Cate, medical director of the Maastricht thrombosis anticoagulation clinic and coeditor in chief of *Thrombosis Journal*, says that major bleeds have serious consequences.

"Large bleeds mostly occur in the gastrointestinal tract and can be lethal if substantial blood loss occurs, especially in elderly subjects with comorbidity; this can be a devastating complication," he says.

Any changes to the ROCKET-AF trial will have a broader effect on the literature.

Carl Heneghan is an author on a forthcoming Cochrane Collaboration review of "direct thrombin inhibitors and factor Xa inhibitors for atrial fibrillation," which includes the ROCKET trial.

He has written to Duke to ask if the results for the main outcome measures in the reanalysis are the same as in the original published paper and, if not, what the differences are after the reanalysis.

A spokesperson for Duke did not answer the question but said that the ROCKET-AF executive committee "intends to publish a full description of its analysis as rapidly as possible."

You should require that the devices used in trials are clearly identified in your publications
Thomas Marciniak

Independent oversight

But given the lack of clarity over the outcomes and the methods used, is a reanalysis by Duke enough?

Marciniak is unequivocal. He says that he would not rely on any reanalyses done by Duke, Johnson and Johnson, or the FDA.

"Because they already missed the problems both in the trial and with the public marketing, I would not trust them to publish anything that is accurate—or that provides any details," he told *The BMJ*.

He added that the datasets need to be released as "the only solution that would lead to unbiased analyses."

But previous attempts to do this have been thwarted.

Krumholz has approached Johnson and Johnson for access to the trial data. His Yale University Open Data Access (YODA) project has an agreement with Johnson and Johnson to make all of the clinical trial data available for its approved products. However, although the company agreed to allow access to the data, Bayer refused.

"This is an ideal situation for data sharing. The evaluation of the data in this trial should not go on behind the curtain. And it seems imprudent to allow those who conducted the trial to be the only ones who can touch the data," Krumholz says.

But it doesn't look like the data release is going to be sanctioned by Bayer any time soon. A spokesperson for the company told *The BMJ* that this is because they have signed up to sharing information only on "study reports for new medicines approved in the US and the EU after January 1, 2014."

Good outcome for patients?

But in the end might this series of errors lead to a favourable outcome for the regulators—and perhaps patients?

At the end of 2015, both the EMA and the FDA held meetings to discuss the need to measure blood levels of direct oral anticoagulants and adjust the dose accordingly to maximise benefit and minimise harm—despite all the manufacturers claiming that this is not necessary. The meetings were held after *The BMJ* revealed that Boerhinger Ingelheim, manufacturers of dabigatran, withheld analyses from the regulators that showed how many major bleeds could be prevented by monitoring anticoagulant activity and adjusting the dose.[14]

A presentation to EMA last year by Robert Temple, deputy director for clinical science at the FDA's Center for Drug Evaluation and Research, suggests that the FDA believes there is a scientific argument for measuring the blood levels of these drugs and adjusting the dose.

"Being too low leads to a stroke, a very bad outcome, and being too high leads to major bleeds, also bad, so that early optimization [of the dose] seems worthwhile," he said adding that direct oral anticoagulants are "very good, but could probably be better."

But once a drug is on the market, regulators lack a mandate to act unless there are safety concerns. However, according to Powell, depending on the outcomes of any reanalysis of the ROCKET-AF trial, this might allow them to take action.

"After a drug is approved, it usually takes a safety signal to prompt significant action on the part of the FDA. It is this lack of safety signal that appears to be hindering the FDA in their desire to pursue tailored dosing for DOACs. If it turns out that the issue with the [INR] device changes the safety profile of rivaroxaban, this may constitute the safety signal necessary for the FDA to act in this regard," he said.

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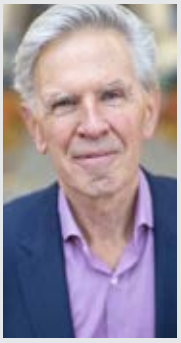
DEVICES USED IN OTHER TRIALS

Given the lack of publicly available information about the point of care testing devices used in the other direct oral anticoagulant trials, *The BMJ* sought to find out what they are.

Lars Wallentin (right), corresponding author of the phase III ARISTOTLE trial (Apixaban versus Warfarin in Patients with Atrial Fibrillation)[6] said that the trials used the ProTime POC device made by International Technidyne Corporation, Edison, NJ, USA.

Daiichi-Sankyo, the manufacturers of edoxaban, also said that the ProTime POC device was supplied to all study sites in the Edoxaban versus Warfarin in Patients with Atrial Fibrillation Trial (ENGAGE AF)[7] and in its venous thromboembolism trial.



How does leadership differ from management?

Matthew Limb untangles these closely related roles

"Leadership" and "management" are so often used interchangeably in discussions about the health service that any distinction between the two roles is often lost.

Michael West, head of thought leadership at the health think tank the King's Fund, believes that management is about "supporting, resourcing, and facilitating day to day work," whereas leadership "creates direction, alignment, and commitment." He says, "The two are interlinked, and it is slightly artificial and misleading to separate them out and treat them as distinct. Leaders must manage to be effective, and management very much involves leadership."

Lisi Gordon, a research fellow at Dundee University's Centre for Medical Education, says, "Management is absolutely about process: the day to day to running of known processes. Leadership is more about change: it's more about continuously reviewing and exploring possibilities for improvement and change."

Jonathan Fielden, medical director at University College Hospital, London, agrees. "Leaders without management skills rarely become good leaders, and managers without the ability to lead people rarely can achieve what they need to," he says. In practice, most senior roles demand both management and leadership qualities, whether these are informal roles or formal roles such as medical director, chief executive, consultant, clinical leader.

He adds, "It's really important, particularly for doctors, that they understand that they have both leadership and managerial responsibilities whatever their roles are. Individuals do tend to move more towards one than the other, but you need both skill sets."

Creative thinking about roles

Doctors who want to be leaders can sometimes feel that they are being sucked into the business of just managing because of political, budgetary, and other pressures. Gordon says, "I can understand how there may be a feeling that people get bogged down with the day to day management, the processes." But she believes that people need to step back and think more creatively about their roles and regard the wider service they provide.

Peter Wilson, a fellow of the Health Foundation's Generation Q leadership development programme, says, "I don't believe that in a good organisation management and leadership are separate." As clinical director at Southampton Children's Hospital, he says that he is managerially held accountable for targets and performance but also leads a "change agenda."

In practice, most senior roles demand both management and leadership qualities

Doctors may tend to see themselves "as leaders but not managers," but that thought process has to change, Wilson says. "Actually, everybody is a leader and a manager simultaneously, because they are managing situations and leading situations. I think it's a cop-out to pretend we're not. It's a way of dodging the bullets as it were. Leadership has to be about how you look at situations, utilise the data that you've got . . . and

FIVE FACTS ABOUT PRIVILEGE AND MEDICINE IN THE UK

1 Disadvantaged pupils are less likely to apply

UK secondary school pupils from disadvantaged backgrounds are less likely than other pupils to apply to study medicine and are less likely to be accepted when they do. A study from the University of Dundee published in January 2016 showed that more than a fifth of all medical school applicants lived in the most affluent areas of the country.

2 Affluent social groups are over-represented

Data from the Medical Schools Council show that students from the most advantaged backgrounds make up 29% of those starting medical school. The council says that this compares with 1% of students from the most disadvantaged backgrounds.

3 As are pupils from private school

Figures from the Higher Education Statistics Authority show that a quarter of medical students in the first year of their first degree have had a private school education, despite these schools educating just 7% of pupils across the UK.

4 Private school students perform less well

Students from private and grammar schools perform less well at medical school than students from non-selective schools. Research published in *BMC Medicine* of the first year exam results of 4811 students at 12 UK medical schools found that students from grammar and private schools did less well than those who were educated at non-selective schools.

challenge where it needs to be challenged."

Stephen Gillam, a GP and lecturer at Cambridge University's Institute of Public Health, admits that he has "never got too hung up about the demarcation" between leadership and management.

But he believes that the current desire to aim for "distributed leadership," which he interprets as "telling doctors you're all leaders now," risks underplaying or "sanitising" a salient characteristic of leadership. "Proper leadership requires sticking your head up above the parapet in a rather more prominent way and is more than just doing the things we all do like leading teams," he says.

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5 They are also less likely to become GPs

Junior doctors who attended private schools are less likely to enter general practice training than those from state schools. A report published by the Centre for Health Economics report in December 2015 showed that trainees from better-off socioeconomic backgrounds were "less likely to be based in general practice than in any other specialty."

How the GMC handles complaints

Marika Davies explores the journey of a complaint

The General Medical Council investigates serious concerns about a doctor's fitness to practise and can take action to remove or restrict a doctor's registration if it concludes that a doctor's fitness to practise is impaired.

Why do patients complain to the GMC?

Patients or their representatives may complain about any aspect of the care they have received from a doctor, such as a delay in diagnosis or if they are unhappy about the doctor's manner and attitude. They may also complain about their overall treatment at a hospital, practice, or clinic, in which case the GMC will take steps to identify the doctors involved. The patient may already have followed local complaints procedures or may choose to go straight to the GMC with the complaint.

Who else can complain to the GMC?

Employers, locum agencies, contracting bodies, and private healthcare providers may raise concerns about issues relating to a doctor's performance, health, or conduct. A referral to the GMC may be made at the same time that local procedures are being followed to investigate the concerns, or the referral may be the outcome of a disciplinary process. The police are likely to share information with the GMC about drink driving offences by doctors or if they are the subject of a criminal investigation. Coroners can refer a doctor to the GMC if they consider that it would prevent a recurrence of the incident that caused the death. Other professionals may notify the GMC of concerns about a doctor. For example, a solicitor may complain about a doctor acting as an expert witness, or a pharmacist may report doctors who are prescribing drugs to themselves. Another regulatory body, whether in the UK or overseas, with which a doctor is registered may also share information with the GMC.

What happens when the GMC receives a complaint?

The GMC reviews all complaints it receives and identifies those that raise potentially serious issues. Its over-riding obligation is to ensure the safety of patients. When it is clear from the outset that the complaint is about matters that could not raise an issue of impaired fitness to practise—for example, a minor non-clinical matter or a minor motoring offence not involving drugs or alcohol—the GMC will normally close the case without taking any further action. It usually investigates only those concerns that could require it to take action to remove or restrict a doctor's right to practise.

Marika Davies, medicolegal adviser, Medical Protection
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PETER LOCKE

Mark Porter, 53, is a GP with a high media profile. He presents BBC Radio 4's flagship medical series *Inside Health*, is a reporter for the *One Show*, and is medical correspondent for the *Times*. He is in practice at Wotton-under-Edge in Gloucestershire, where the sight of a patient waving one of his cuttings must be a frequent experience. Porter also applies his healing hands to old cars, confessing that, if he was exiled to a desert island and was not allowed to take his wife, he'd settle for a Porsche 911 of 1970 vintage and the tools to tinker with it. He isn't the BMA chair; that's a different Mark Porter.

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Mark Porter
A covert petrolhead

What was your earliest ambition?
To marry Gerry Knight, but I was only 5.

Who has been your biggest inspiration?
Too many to single out one person. As a doctor I meet a lot of people in difficult circumstances—a fertile ground for inspirational acts. And the less fuss they make, the more likely I am to be inspired.

What was the worst mistake in your career?
From a media perspective, it was turning down an offer from Columbia TriStar to host a show in the United States.

What was your best career move?
Joining *GP* magazine. There I answered a phone call in 1992 from a BBC producer looking for a doctor to join the team behind *Good Morning*. I knew just the bloke.

Bevan or Lansley? Who has been the best and the worst health secretary in your lifetime?
Bevan was best. I prefer to keep my opinion of health secretaries to myself: it makes it easier to interview them (on the rare occasions they agree to talk to me).

Who is the person you would most like to thank, and why?
Simon, the surgeon who saved my mother's life. He knows who he is.

If you were given £1m what would you spend it on?
A flat in Fitzrovia (if you can get one for a million).

Where are, or were, you happiest?
At home in the Cotswolds.

What single unheralded change has made the most difference in your field?
The internet.

Do you support doctor assisted suicide?
Yes, as a patient. But I'm not sure that I could get involved as a doctor.

What book should every doctor read?
Do No Harm, by Henry Marsh.

What poem, song, or passage of prose would you like mourners at your funeral to hear?
The haka, performed by the All Blacks. And William Henry Davies's poem *Leisure*, which starts: "What is this life if, full of care, we have no time to stand and stare." I would love to have faced the haka—and to have had time to stop and stare.

What is your guiltiest pleasure?
The pub. And apple strudel. Although not at the same time.

If you could be invisible for a day what would you do?
Avoid anyone I know, for fear of seeing or hearing something I wish I hadn't.

What is your most treasured possession?
Sadly, it's my car. I'm a covert petrolhead.

Summarise your personality in three words
Inquisitive. Restless. Particular.

Where does alcohol fit into your life?
It's been a cornerstone of much of my social life—in reasonable quantities.

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