GPs call for ballot on protest action

GPs have called on the BMA to ballot the profession on their willingness to take industrial action and to sign undated resignation letters.

GPs at the BMA’s conference of local medical committees (LMCs), the bodies that represent GPs at a local level, in London on Friday 20 May said that the government’s General Practice Forward View, published last month, was not an adequate response to the BMA’s “urgent prescription for general practice.” A motion said that GPs considered this to be “sufficient grounds” for a trade dispute and that unless the government accepted the urgent prescription within three months the BMA should ballot GPs on their willingness to take industrial action.

They also voted for the BMA to ballot the profession on their willingness to sign undated resignation letters.

The motion also called for the association to ballot GPs on what forms of industrial action they would be prepared to take and to produce a report for practices on which type of industrial action wouldn’t breech their contracts.

Proposing the motion, Jackie Applebee, from Tower Hamlets LMCs, said, “We are at a very, very serious moment. No one even wants to consider industrial action, but today it was announced that the NHS is £3bn in deficit. How much worse can it get? How much more are we going to have to talk to government before they provide any meaningful support for general practice?”

Kieran Sharrock, from Lincolnshire LMC, said that his LMC had already balloted its members. “They want industrial action. They don’t want to resign: they can’t afford to resign, but they want industrial action.”

Commenting on the debate, Chaand Nagpaul, chair of the General Practitioners Committee, said, “I think it is right that we do find out from the profession exactly their intent.” And commenting on potential industrial action, Nagpaul said, “We need a narrative, and what the juniors had was a very clear narrative about weekend working, about the impossibility of trying to extend five days into seven, and the unfairness of not recognising premium days and out of hours.

Nagpaul added: “This motion... gives us an opportunity to understand exactly what GPs are prepared to do.”

Abi Rimmer, BMJ Careers

Cite this as: BMJ 2016;353:i2900

Chaand Nagpaul, chair of the BMA’s General Practitioners Committee, said that it was right to “find out from the profession exactly their intent”
UK news
Agreement is reached on junior doctors’ contract
Junior doctors will vote from 17 June to 1 July on whether to accept the latest contract on their terms and conditions, and the result will be made known on 6 July. The BMA and the government agreed the details of the new contract on 18 May after 10 days of talks (full story doi:10.1136/bmj.i2853). For more coverage on the junior doctor contract see pages 342 and 343.

Tobacco firms fail to stop plain packaging
Plain packaging of tobacco products in the UK came into force on 20 May, the day after a judge in the High Court dismissed a legal challenge by the world’s four biggest tobacco manufacturers. Mr Justice Green said in his ruling, “The essence of the case is about whether it is lawful for states to prevent the tobacco industry from continuing to make profits by using their trade marks and other rights to further what the World Health Organization describes as a health crisis of epidemic proportions and which imposes an immense clean-up cost on the public purse. In my judgment the regulations are valid and lawful in all respects.”

Incentivising GPs does not affect mortality
The NHS Quality and Outcomes Framework (QOF)—the world’s largest pay-for-performance scheme in primary care—has not improved mortality rates from the chronic conditions targeted by the programme, including cancer, diabetes, and heart disease, a study showed (full story doi:10.1136/bmj.i2882).

Academics warn of “Brexit” threat to NHS
A group of leading academics, writing in the Journal of the Royal Society of Medicine, argued that the NHS would get less money if the UK left the EU because the Treasury estimates that tax receipts could be lower by £36bn a year. Around 50 000 people work for the NHS, including 9000 doctors, and their continued employment “would be uncertain, as would be the future recruitment of workers from Europe.”

Use mefloquine for troops as “last resort”
British military personnel should be given the antimalarial drug mefloquine (Lariam) only as a “last resort,” MPs have concluded.

In a report into the use of the drug among the armed forces, the House of Commons Defence Committee accused the Ministry of Defence of displaying a “lamentable weakness in [its] duty of care towards service personnel” and of ignoring the “stringent conditions” for safe prescribing set out by the drug’s manufacturer, Roche.

“We see no reason to disbelieve the very strong anecdotal evidence that such conditions have been ignored in dispensing it to large numbers of troops about to be deployed. Indeed, it is hard to see how they could ever be met except when the numbers to be individually assessed are few and far between,” said the report. “It is our firm conclusion that there is neither the need nor any justification for continuing to issue this medication to service personnel unless they can be individually assessed, in accordance with the manufacturer’s requirements.”

Caroline White, London  Cite this as: BMJ 2016;353:i2946

Zika virus
Zika risk in Europe
The overall risk of Zika virus transmission in Europe this spring and summer is low to moderate, the WHO said. But it warned that Georgia, Madeira (below), and the southern part of the Russian Federation are at high risk of the disease. A moderate risk of spread was found in 18 countries, primarily in the Mediterranean basin, including France, Greece, Italy, Spain, and Turkey (full story doi:10.1136/bmj.i2887).

WHO quells call to cancel Olympics
Calls to cancel this summer’s Olympic Games in Brazil for fear of accelerating a global spread of the Zika virus were quelled by new WHO guidance. Amir Attaran, of the University of Ottawa in Canada, described Rio de Janeiro as being at the “heart” of the current Zika epidemic and said that the Olympic organisers must postpone or move the games. But WHO’s guidance advised athletes and visitors to practise safe sex, choose air conditioned accommodation, use insect repellent, and wear light coloured clothing covering the body (full story doi:10.1136/bmj.i2899).

Research news
Bariatric surgery for type 2 diabetes
Bariatric surgery should be included in guidelines for people with type 2 diabetes and obesity, diabetes societies recommended in a joint statement, for the first time recognising surgery as a therapeutic intervention for such patients. The societies agreed that surgery should be recommended to treat type 2 diabetes in all patients with a body mass index (BMI) above 40.0 and in those with BMI 35.0-39.9 where hyperglycaemia is inadequately controlled, and it should be considered for patients...
with BMI 30.0-34.9 where hyperglycaemia is not controlled despite optimal treatment (full story doi:10.1136/bmj.i2955).

Childhood environment link to cancer risk
A rapid review provided more evidence of a link between children’s surroundings and their risk of cancer later in life. People brought up in the poorest households had a greater risk of stomach and lung cancer in later life, and some evidence showed an increased risk of colorectal, liver, cervical, and pancreatic cancers in people with a lower childhood socioeconomic position (full story doi:10.1136/bmj.i2808).

Aspirin after stroke reduces further events
Taking aspirin cuts the risk of recurrent ischaemic stroke by nearly 60% in the six weeks after a transient ischaemic attack (TIA) or ischaemic stroke, but the benefit then declines to no effect by 12 weeks, a study in the Lancet found. "Medical services should give aspirin as soon as possible [after suspected TIA or stroke] and public education should be aimed at self administration after unfamiliar transient neurological symptoms suggestive of threatened stroke,” said the researchers (full story doi:10.1136/bmj.i2876).

Antibiotics Drug firms “should get $1bn” for new antibiotics
Drug companies should get rewards of more than $1bn (£692m) for each new antibiotic they bring to the market, said the final report of a review on antimicrobial resistance. It said that some $40bn should be spent in the next decade to fight antimicrobial resistance and proposed a levy on the drug industry, which could be avoided by companies that invest in research (full story doi:10.1136/bmj.i2863).

Life expectancy People living five years longer on average
Global life expectancy has increased by five years since 2000 to 71.4 years for children born in 2015, according to WHO. However, while life expectancy for newborns in 29 high income countries was at least 80 years, in sub-Saharan Africa it was less than 60 years. Japan had the highest life expectancy (83.7) and Sierra Leone the lowest (50.1). The US had the fourth highest life expectancy in the Americas (79.3), after Canada, Chile, and Costa Rica. The UK’s life expectancy was 81.2. (full story doi:10.1136/bmj.i2886).

Incentives to drug companies may help to boost the antibiotics pipeline, says a new report

Teen pregnancies
Conception rates among women aged 15-17 in England fell from a peak in 1998 of approximately
47 per 1000 to fewer than 25 per 1000 in 2013

Is someone leading us up the garden path?
You may scoff, but a new report (http://bit.ly/1TEIPk8) has found that putting the rake and secateurs to use improves mental and physical health at all ages.

Who wrote the report?
It’s by the well respected think tank the King’s Fund, which usually concerns itself with thornier issues such as the NHS deficit.

OK, show me this evidence
The report found that gardening at schools significantly increased children’s fruit and vegetable intake. Among adults, allotment gardening has been shown to improve mood, self esteem, and cortisol concentrations (which can be associated with acute stress). And in people with depression and anxiety gardening reduced symptoms and improved social functioning.

How does this relate to the NHS?
The report argues that there is much that the NHS and social care system can do to take advantage of people’s love of gardening. Clinical commissioning groups could include gardening in social prescribing projects. Up to a fifth of GPs’ time is spent on problems with social causes, so an option that improves health without prescribing seems attractive.

How could this work in practice?
In London the Lambeth GP Food Co-Op is one example of many flourishing projects. It has created a network of gardens at 11 general practices and King’s College Hospital where GPs, nurses, and patients grow food and vegetables and discuss diet and nutrition.

Come into the garden, Maud . . .
One of the GPs in the Lambeth project, Vikesh Sharma, said, “It provides the only platform for me as a GP to see my patients outside the physical walls of my surgery, reinforces the idea of community doctors, and reminds me of the wider context of what being healthy actually means.”

Susan Mayor, London
Cite this as: BMJ 2016;353:i2951
Regulator will do fewer inspections as budget is cut

Providers of health services in England will be inspected less often and in less depth if they are considered to be performing well, under plans by the NHS regulator the Care Quality Commission to streamline its operations. But doctors' leaders have said that the planned changes do not go far enough in reducing the burden of inspection on clinicians.

The CQC published its five year strategy for 2016 to 2021 on Tuesday 24 May, in which it said that it wanted to bring in a more “targeted, responsive and collaborative” approach to regulation.

A key change in its approach will be a move towards better use of information from the public, healthcare providers, other regulators, and oversight bodies to allow resources to be targeted at places considered to have the highest risk to quality of care.

This means that there will be longer intervals between inspections for general practices rated “good” or “outstanding,” of as much as five years rather than the original intention of doing so every two years, if practices can continue to show that they are providing good care. At NHS trusts and foundation trusts, those with good ratings will continue to have annual inspections, but these will have a more targeted and tailored approach focused on core services, while large scale, comprehensive inspections will still take place at sites that are considered to need them.

Deficit in NHS provider sector triples in a year to £2.45bn

Providers of NHS services have amassed an unprecedented £2.45bn deficit in the past year, and although the scale of deficit is not as bad as feared, it has still almost tripled from the previous year (£834m), despite additional funding for the NHS and major efforts to boost efficiencies.

The figures, published on 20 May, show that for 2015-16 around two thirds (65%), or 157 of 240 NHS provider organisations, reported a deficit, most of which were acute care trusts.

NHS Improvement, the body responsible for overseeing trusts, said that overall the NHS provider sector was £461m worse off than planned but against record breaking demand. Providers made £2.9bn in efficiency savings while under continuing pressure from further increases in demand, including a record 21 million emergency patients last year, problems discharging medically fit patients, and high costs, particularly of agency staff. Consequently, many providers missed the national waiting time standard for emergency care and other operational performance measures in the last three months of 2015-16. The sector spent £3.64bn on agency and contract staff in 2015-16.

Halfway through 2015-16 the sector reported a deficit of £1.6bn and then predicted an end of year loss of £2.8bn, so the actual figures were not quite as high as feared. Some savings had been achieved, said NHS Improvement, such as measures to spend £300m less than planned on agency staff since October 2015 and a reduction of £86m from a year ago in spending on management consultants.

Jim Mackey, chief executive of NHS Improvement, said, “Providers have made every effort to meet rising demand for services at a time when the sector is also being asked to be more efficient than ever.”

MARK PORTER
BMA COUNCIL CHAIR

“We must draw up a long term strategy for the NHS that addresses the fundamental workload and funding challenges that are overwhelming our health service. Failure to invest now will result in a disaster in the future both financially and in terms of patient health.”

There will also be more targeted unannounced inspections, made on the basis of information that is constantly updated, of places where there has been a sharp rise in numbers of people reporting poor care from a particular service.

The report says, “Our overall budget will reduce by £32m by 2019-20 [from £249m in 2015-16 to £217m in 2019-20], so we need to deliver our purpose with fewer resources.”

Other changes include developing a shared dataset with partners, other regulators, and commissioners, so that providers are asked for details about care quality only once.

Richard Vautrey, deputy chair of the BMA’s General Practitioners Committee, said, “GPs have major terms of patient health.”

CHRIS HOPSON
CHIEF EXECUTIVE OF NHS PROVIDERS

“There is now a clear gap between the quality of health service we all want the NHS to provide and the funding available. What we can’t keep doing is passing that gap to NHS trusts—asking them to deliver the impossible and chastising them when they fall short. Not least because it is placing an increasingly intolerable burden on NHS staff whose commitment and discretionary effort are the lifeblood of our NHS.”

Cite this as: BMJ 2016;353:i2904
THE CQC’S BUDGET will be cut by £32m in the next four years from £249m in 2015-16 to £217m by 2019-20

concerns about the CQC and would want to see a much more significant reduction to the burden of registration and inspection than what is being proposed—and in particular abandoning the nitpicking clipboard approach to inspections and scrapping the evidence free simplistic rating scale. “They have talked about reducing the number and frequency of inspections before and moving to greater reliance on remote monitoring, but this means that they should make significant reductions to the cost of regulating general practice. And this should be reflected in a cut to the fees unreasonably imposed on practices.”

The BMJ

Richard O’Dowd London
Cite this as: BMJ 2016;353:i2979

News from the LMC conference, 19-20 May

GPs back move to charge overseas visitors
GPs at the BMA’s conference of local medical committees (LMCs) voted to carry a motion calling for foreign visitors to be able to attend UK general practices but “only on a private fee-paying basis.”

Plans to charge overseas visitors for accessing GP services were announced in the Queen’s speech on 18 May. In response, the Royal College of General Practitioners said that it was “disappointed and frustrated” that the government intended to push ahead with the plans.

Russell Brown, of East Sussex LMC, proposed the motion to back the government on charges for overseas visitors. He said, “This motion is not about denying care. It is about proper resourcing of work that is currently unfunded. When a GP is seeing a foreign visitor, that is time they cannot devote to their NHS patients.”

Cap on locum GP fees is rejected
GPs rejected a cap on fees charged by locum doctors and said that locums and general practices should be able to agree terms and conditions mutually.

Faisal Baig, from the sessional GP subcommittee of the BMA’s General Practitioners Committee, proposed the motion. He said that locums kept many afloat by covering maternity and sick leave and other gaps in rotas. He said that the idea of one indicative rate for a variety of locum jobs was nonsensical. “The indicative rate idea was revealed soon after the agency locum cap was introduced into secondary care. It hasn’t worked there, and it won’t work here.” Baig added, “We need to look at the bigger picture, which is: there is a workforce problem, [and] bringing in the cap will only make that worse.”

Channel extra funding to weekend emergency cover
GPs have urged the government to abandon its push for routine seven day services in primary care and instead to channel any additional funding into emergency cover at weekends.

Christopher Browning of Suffolk LMC, who proposed the motion, said that many practices were struggling to provide services five days a week. Browning said that GPs could not provide routine services at weekends without staff to support them. He said that his own practice was “on its knees” and that the idea of removing staff and resources from weekdays to cover weekend working “doesn’t bear thinking about.”

“The only people who really think there is a demand for this are sitting down the river in Westminster,” he said.

Richard Murray
Director of Policy at The King’s Fund

“Overspending on this scale is not down to mismanagement or inefficiency in individual trusts—it shows a health system buckling under huge financial and operational pressures. At the same time, performance against key targets is deteriorating and concerns about quality of care are increasingly widespread. The challenge facing the NHS is not limited to hospitals: general practice is also in crisis as they try to keep up with demand.”

Simon Stevens
Chief Executive of NHS England

“For the year that we are now in we have got the funding increases that we need to kick start the changes that the health service needs to bring about, and we are, on the back of that, clearly going to be able make substantial inroads to the hospital deficits.”

The BMJ

Gareth Iacobucci, Abi Rimmer, The BMJ
What’s changed in the proposed junior doctor contract?

**Tom Moberly** looks at how proposals for a new contract for junior doctors have changed after last week’s announcement of a deal between the government and the BMA

**WEEKEND WORK**

Junior doctors will not have to work more than one in two weekends, and those who work more than one weekend a month will get additional pay. There will be five levels of pay supplement, from 3% for those working one weekend in eight to 10% for those working one weekend in two. There will also be an on-call availability allowance of 8% and an average basic pay increase of somewhere between 10% and 11%. The exact size of this increase will depend on the outcome of final modelling calculations.

**PATIENT SAFETY**

Doctors who work beyond the hours described in their work schedule in order to fulfill professional duties to patient safety will be paid or given time off in lieu to compensate for that work, as long as the work is authorised. Work can be authorised in advance, during a shift, or in retrospect, and employers will be required to bring in systems that make it simple for doctors to make claims. If a claim is not authorised the reason for this decision will be explained to the doctor and to the guardian of safe working, who will act as the champion of “safe working hours” for junior doctors. Junior doctors will also have an opportunity to assess the performance of the guardians of safe working through a system of 360° appraisal.

**PARENTAL RESPONSIBILITIES**

Trusts will be required to consider caring and other family responsibilities when designing rotas. Doctors who change specialties because of caring responsibilities will have their pay protected. A catch-up programme of accelerated training support will be introduced for doctors who take extended leave, including maternity leave. This support will include mentorship, study leave funding, and special training schemes.

**MEDICAL COUPLES**

Health Education England will be given a duty to consider family responsibilities when it makes decisions on the allocation of training rotations. It will also have to review how medical training can be reformed to enable couples who are both trainee doctors to apply to train in the same area and those with caring responsibilities to train close to their home.

**WORKING PATTERNS**

After a run of three night shifts, doctors will be guaranteed a 48 hour rest period. Shifts that start after 8 pm, last more than eight hours, and end by 10 am the next day will attract an enhanced pay rate of 37% for all hours worked. Fines will be imposed on trusts if, over a four week period, any doctor is not able to take at least three quarters of their breaks.

**SENIOR DECISION MAKERS**

A new role of “senior clinical decision maker” will be introduced, and doctors taking on this role will be given additional pay. The role will be applied to experienced junior doctors who are able to assess whether patients need to be admitted to or discharged from hospital at weekends.

**WHISTLEBLOWING**

The contract enshrines the right of junior doctors to raise concerns and be protected for doing so, in line with legislation on whistleblowing in the public interest. Junior doctors will also be able to raise concerns about the work of Health Education England without this having any effect on their treatment by them or their employer.

**CHANGING SPECIALTIES**

Doctors will be able to move specialties more easily. This will be achieved by developing systems that allow skills and competencies that junior doctors have developed in one specialty to be recognised as part of training in another specialty. The General Medical Council will work with medical royal colleges, junior doctors, and funders of postgraduate medical education to support the recognition of competence when doctors change training paths.

**LOCUM WORK**

The contract agreement states that junior doctors can undertake locum work above and beyond the hours in their work schedule. However, those wishing to do so must “offer such additional hours of work exclusively to the service of the NHS via an NHS staff bank,” the agreement says.

Johann Malawana (above), chair of the BMA’s Junior Doctors Committee
What happens now with the contract?

31 May 2016
Full details of contract published

17 June to 1 July 2016
Junior doctors balloted on whether to accept new contract

6 July 2016
Deadline for announcement of ballot results

October 2016
First tranche of trainees move to the new terms and conditions

March 2017
GMC completes work on allowing doctors in training to move between specialties more easily

April 2017
Second set of trainees transition to the new terms and conditions

August 2017
All remaining existing trainees and new entrants move on to the new terms of conditions

August 2018
BMA and NHS Employers jointly commission review of new contract

The BMA, the government, and NHS Employers complete review of the role of guardians of safe working

BMA to explain contract details through June road shows

Details of the new contract deal will be explained to junior doctors in a series of road shows that the BMA will be holding across England in early June.

The full terms and conditions of the new contract will be published on 31 May, alongside an equality impact assessment of the revised agreement. Junior doctors will be balloted on whether to accept the new contract between 17 June and 1 July.

The BMA will be seeking to persuade junior doctors to vote to accept the deal agreed with the government last week after 10 days of talks facilitated by the conciliation service Acas. Commenting on the agreement of the Acas settlement, Johann Malawana, chair of the BMA’s Junior Doctors Committee, said that the BMA was pleased to have reached an agreement.

“Junior doctors have always wanted to agree a safe and fair contract, one that recognises and values the contribution junior doctors make to the NHS, addresses the recruitment and retention crisis in parts of the NHS, and provides the basis for delivering a world class health service,” he said.

“I believe that what has been agreed today delivers on these principles, is a good deal for junior doctors, and will ensure that they can continue to deliver high quality care for patients. This represents the best and final way of resolving the dispute, and this is what I will be saying to junior doctors in the weeks leading up to the referendum on the new contract.”

Simon Wessely, chairman of the Royal College of Psychiatrists, said he suspected that junior doctors would not be satisfied with every part of the agreement. “No negotiated settlement ever gives anyone everything they want,” he told junior doctors in a blog post. “There is always compromise.”

“Dr Malawana, who has clearly negotiated long and hard, has delivered more than most people can have expected. Of course he won’t be happy with everything, and I suspect nor will you.”

He added, “If this offer is accepted then most of you will, like myself, feel a sense of relief. This will be shared by the vast majority of the public and our patients and carers . . . We cannot know what might happen should the action continue and I fervently hope we will never find out.”

Sarah Wollaston, conservative MP and chair of the parliamentary health select committee, said that the dispute over the new contract would not be resolved unless junior doctors agreed to the revised proposals. “We are not out of the woods yet,” she said. “We need junior doctors across the country to vote for this agreement in a referendum.”

Tom Moberly, BMJ Careers
tmoberly@bmj.com

“No negotiated settlement ever gives anyone everything they want, there is always compromise”
Simon Wessely

“We are not out of the woods yet. We need junior doctors across the country to vote for this agreement in a referendum”
Sarah Wollaston
Herbs for a hospice

The Modern Apothecary, a garden at this year’s Chelsea Flower Show, has been designed for patients and families using St John’s Hospice in London, where it will ultimately be relocated.

The herb farmer Jekka McVicar, who has been dubbed the Queen of Herbs, wanted to create a space to prompt quiet reflection but which could also inspire and challenge and was rich in sensory stimulation.

Plants include herbs such as borage, bay, caraway, nasturtium, and rosemary, that have long been used as traditional remedies.

McVicar took inspiration from conversations with the Devon GP Michael Dixon about plants and health. She said, “The simple act of sitting within a garden, surrounded by plants, has a calming effect and can lift spirits.”

The garden incorporates a sculpture of the serpent entwined rod of Asclepius, a Greek god associated with healing.

St John’s Hospice in St John’s Wood provides palliative care to more than 3000 terminally ill patients a year without charge. Chelsea Flower Show runs till 28 May.

See www.jekkasherbfarm.com

Richard Hurley, features and debates editor, The BMJ

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NEWS, p 339
editorial

Money back guarantees for non-reproducible results?

Better solutions exist to research’s “reproducibility crisis”

Mone y back guarantees are unheard of in biomedicine and healthcare. Recently, the US provider Geisinger Health System, in Pennsylvania, started a programme to give patients their money back if they were dissatisfied.¹ Soon thereafter, the chief medical officer at Merck launched an even bigger surprise, proposing an “incentive-based approach” to non-reproducible results—what he termed a “reproducibility crisis” that “threatens the entire biomedical research enterprise.”²

The problem of irreproducibility in biomedical research is real.³⁻⁴ In the same vein, the retraction of academic papers has been rising, attributable to irreproducible results and falsified data.⁵ This problem is not confined to basic science or animal model work from academic laboratories. Clinical trials, the final common pathway for the validation and approval of new drugs, have been plagued with serious drawbacks.

The bad science in clinical trials has been well documented and includes selective publication of positive results, data dredging, P hacking, HARKing, and changing the outcomes that were prespecified at the beginning of the study (box).⁶⁻⁷ Furthermore, the disparity between what appears in peer reviewed journals and what has been filed with regulatory agencies is long standing and unacceptable.

Thus, the proposal from a senior executive at Merck to set up a “clawback” model, whereby an academic institution would refund its financial payment if the basic science or preclinical results prove to be irreproducible, is ironic. When I was involved in exposing the dangers of Merck’s rofecoxib (Vioxx) in 2001,⁹⁻¹⁰ the company exemplified nearly every aberration listed for clinical trials. Although the executive making the proposal was not with Merck during the rofecoxib era, and the idea is said not to represent the company’s position, it is hard to miss the threads and the twist.

As far as I know, the problems of irreproducibility in the clinical trials of rofecoxib never led to any money being given back to the millions of patients who were unwittingly exposed to the risk of cardiovascular side effects. Furthermore, medications are much less clinically effective than generally acknowledged. The top 10 prescription drugs in sales have a cumulative clinical response rate of less than 20%.¹¹

There is also the concern that reproducibility is not a simple story. For example, one of the biggest breakthroughs in biomedicine was Yamanaka et al’s success in inducing pluripotent stem cells.¹² It took the most experienced stem cell researchers in the world well over a year to reproduce the findings. Even the cost of $500 000 (£342 000) to $1m cited by Rosenblatt to replicate findings at Merck might be wholly inadequate. It’s not just money that buys replication; time and experience can come into play. Furthermore, it’s not dichotomous. There’s partial replication. Should industry get a partial refund proportionate to the number of experiments replicated?

Transparency is key

What is missing is the deep commitment—across academia and the life science industry—for open science and open data. Everyone asks for accountability of research findings, which can be vastly promoted by making them fully transparent. But compliance is poor. Even the mandatory requirement for publishing results on Clinicaltrials.gov within two years was evaded for 87% of 4347 clinical trials in academic centres.¹³

When we start to see all the protocol, prespecified hypotheses, and raw data available for review, along with full disclosure of methods and analyses and what, if anything, changed along the course of experiments, be it at the bench or in clinical trials, we’ll have made substantive progress. A promising, low cost digital solution exists to capture all of the data and promote trust and reproducibility in biomedical research.¹⁴⁻¹⁵ Use of blockchain technology has recently been shown to provide an immutable ledger of every step in a clinical research protocol, and this could easily be adapted to basic and experimental model science. With every step of a research path digitised and shared, we have a platform well suited for rapid, independent verification of methods and results.

Until we develop the right system, we don’t need or want money back guarantees on research reproducibility. But I’d be interested to pick up on that refund offer for my medications or any medical care that doesn’t work.

I’d be interested to pick up on that refund offer for my drugs that don’t work

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Eric J Topol, director, Scripps Translational Science Institute, La Jolla, CA 92037, USA etopol@scripps.edu
Lessons from the fatal French study BIA-10-2474

Do not test in humans drugs that lack an identified therapeutic potential

In January the phase I study of the drug BIA-10-2474 conducted in Rennes, France, left one initially healthy volunteer dead and three with serious neurological damage, some of which may be permanent.1 2

This was a not unusual phase 1 study of a new wannabe drug and included four substudies: single ascending doses, multiple ascending doses, a food interaction study, and some pharmacodynamic testing looking for potential indications.

The study of single ascending doses took place uneventfully up to the maximum dose of 100 mg. The first four series of multiple ascending doses had no problem up to 20 mg for 10 days. Suddenly, on the fifth day of the fifth series (50 mg daily) one participant developed neurological problems and was admitted to hospital. The next day the other participants received the drug. Three of the four remaining participants had neurological symptoms and were admitted to hospital. They recovered, some with severe sequelae, but the first participant died.

No precursor symptoms were seen, but subsequent scans showed a very unusual pattern of lesions in the medulla oblongata and thalamus. About 80 people had previously received the drug, with no neurological symptoms or lesions seen in magnetic resonance imaging.

BIA-10-2474 is a partly irreversible inhibitor of fatty acid amide hydrolase (FAAH), an enzyme involved in the metabolism of the neurotransmitter anandamide. Nevertheless, when FAAH is fully blocked, anandamide will use cyclo-oxygenase and lipooxygenase, resulting in endoperoxides and prostaglandins. Even so, there is no known toxicity of high dose anandamide. Nevertheless, when the first participant was admitted to hospital the study should have been suspended, pending resolution. That might have spared the other participants but would not have saved the first’s life.

An expert committee remains baffled by the extreme reaction, which has no other reasonable explanation than the drug.3 Among the possible causes, that of a threshold effect on other enzymatic pathways seems the most plausible.

**Recommendations**

Beyond the careful monitoring of participants in such studies—and the necessary caution if anything untoward happens, however unusual—the committee put forth several commonsense recommendations:

- When testing drugs that target the central nervous system, complete neurocognitive assessment of the volunteers should be a prerequisite.
- In dose escalation studies there should be enough time between study periods to analyse the data from the previous group before dosing the next.
- In dose escalation studies consider all previously known data, including in human studies, not just preclinical data as indicated in European recommendations.

An international expert committee should be convened to consider the methodology of “first in man” studies and how best to protect participants.

Data from first in man studies should be made public, especially if the drug’s development has been stopped prematurely. But the most important recommendation was the committee’s first: do not test drugs in humans that do not have an identified therapeutic potential. In the case of BIA-10-2474 it would seem that there was no clear target. Perhaps the use of high doses was a fishing expedition to try to find some activity where previous drugs sharing the same purported mechanism of action had failed.

As all drugs are dangerous, even if some of them are useful,4 shouldn’t we ensure at least some potential usefulness of a drug before we expose people to its dangers?

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1. BIA-10-2474 is a partly irreversible inhibitor of fatty acid amide hydrolase (FAAH), an enzyme involved in the metabolism of the neurotransmitter anandamide.
2. Several other FAAH inhibitors have been tested in humans then dropped for lack of effect. BIA-10-2474 was tested for toxicity in four species, but nothing untoward was found other than possible pulmonary toxicity in dogs at very high doses. The kinetics were not linear, with increasing half-lives indicating possible accumulation at higher doses.
3. The drug was classified as not high risk, and the study protocol was not unusual for phase I studies of a non-toxic drug. Perhaps the dose increase in the multiple ascending doses substudy was a little steep (from 20 mg/day in the fourth series to 50 mg/day in the fifth series) and the doses too high: maximal FAAH inhibition was obtained at 3 mg a day, or less. BIA-10-2474 is not very selective for FAAH and at higher doses will inhibit other enzymes, with unknown consequences. When FAAH is fully blocked, anandamide will use cyclo-oxygenase and lipooxygenase, resulting in endoperoxides and prostaglandins. Even so, there is no known toxicity of high dose anandamide.
4. As all drugs are dangerous, even if some of them are useful, shouldn’t we ensure at least some potential usefulness of a drug before we expose people to its dangers?
The BMJ has covered the debate about the so-called “weekend effect” in response to calls for the NHS in England to provide more senior consultant cover at weekends, and subsequent industrial action by the BMA’s junior doctor members. Articles have appeared in the journal, BMJ Careers, and as blog posts, and you can now access them all in one place at bmj.com/weekend.

This new online collection also links to a podcast round table discussion. Analysis editor Navjoyt Ladher asked some of the key academics who have published relevant research to make sense of what we know and don’t know about weekend care in hospitals.

The collection includes Jacqui Wise’s feature, published in print last week, which looks at recent research on the increased risks for patients admitted at the weekend. Wise asked leading experts to point out where there is consensus and where there are gaps.

Here is a selection of responses to her article:

Kuljit Bhogal, a ST6 psychiatrist in learning disabilities based in Wallingford, Oxfordshire, said: “We need to include social care and primary care in the debate about what a 7 day service would or should look like.”

Oscar Jolobe, a retired geriatrician from Manchester, said; “The crucial question is whether or not a seven day service is compliant with the core values of the profession, which include a compassionate recognition of the distress that patients experience when the availability of NHS services such as emergency endoscopy or imaging modalities, is demonstrably not the same at weekends as it is on weekdays.

Brian H Willis, NIHR clinical lecturer in primary care at the University of Birmingham, said: “This has been a politically charged issue which has received widespread coverage in the press and the journal editors need to re-examine whether they have prioritised sensationalism over objectivity.”
Would Brexit mean a return to dangerously long working hours?

**Would working hours change?**
The European Working Time Directive is the key piece of European Union legislation affecting doctors' working hours, limiting the working week to 48 hours. The regulations were implemented in 1998, but all junior doctors were not included until 2009.

Some specialties, particularly surgeons, have been concerned that the 48 hour week limits training. Doctors can opt out of the 48 hour limit, and a Royal College of Surgeons (RCS) review of the directive called for more widespread use of the opt-out. The UK is one of the few EU countries to use the opt-out.

Jason Heyes, professor of employment relations at the University of Sheffield, believes that the Working Time Regulations, the UK law enacting the EU directive, is one of the employment laws most likely to be repealed or reformed if we leave the EU. “The regulations are a particular bugbear as they’re seen by many Conservative politicians as an unnecessary and damaging burden on employers,” he says.

However, the British Medical Association is likely to resist any large increase in hours worked. In a statement published at the time of the RCS review, Mark Porter, BMA council chair, said, “No one wants a return to the days when doctors were working dangerously long hours.”

But Heyes adds, “Without the protection of the legislation, changes in working time and holidays would probably play out differently sector to sector. If the legislation is repealed it might reduce the bargaining strength of trade unions, and workers in non-union environments would have no protection.”

**Would retirement age and pensions change?**
Doctors with an NHS pension are unlikely to see changes if we leave the EU. The rules of the NHS pension scheme are laid down in regulations agreed by parliament, and pensions are funded by taxation rather than relying on investments. Doctors with private pensions may be affected, however. A report from the Society of Pension Professionals said the resulting uncertainty after a vote to leave would be detrimental to financial markets and therefore pensions in the short term. But in the long term Brexit could “create new opportunities for UK pensions to avoid potentially crippling liabilities in the future.”

Like most of their fellow European citizens, UK workers will see their retirement age increase over the coming years. By 2028 it will be 67, rising to 68 by 2046. The UK already has one of the highest retirement ages in Europe, and the trajectory for retirement age is only upwards, regardless of whether the UK is a member of the EU.

**Would maternity rights change?**
Women in the UK have the second longest maternity leave entitlement in the EU. Mothers are allowed to take 52 weeks’ leave (39 weeks of which is paid), well above the EU statutory minimum of 14 weeks. However, it is harder to compare maternity pay, as EU countries’ policies vary greatly. Like most occupational maternity schemes the NHS maternity scheme is more generous than the statutory scheme. Because this is an NHS agreement it is unlikely to be affected by Brexit.

However, other social protections have been introduced by EU law, such as the right to parental leave. This directive, implemented in the UK in March 2013, gives mothers and fathers the right to take 13 weeks’ unpaid leave per child before its 5th birthday. It also gives workers rights to paid leave to look after a sick child or other dependant, although it does not specify how much time should be taken.

The EU has also introduced laws ruling against discrimination on the grounds of disability, age, religion, and sexual orientation. However, Heyes believes there is little appetite in government to roll back on any of these social protections.

“Once these things become embedded and employers start to change their procedures they don’t necessarily clamour for legislation to be repealed,” he said.

**Would Brexit affect my job security?**
Another law based on an EU directive that Heyes believes could be a target for reform or repeal in the event of Brexit is the law governing agency workers. These regulations give temporary workers, including locum doctors, the same working conditions and employment rights as a permanent employee. Again, they are seen by employers to present an unnecessary burden.

In a report assessing the effect of the regulations a year after their implementation the Confederation of British Industry said that businesses’ costs had increased while “positive impacts for temps were unclear.”

Gisela Stuart, a Labour MP who is campaigning to leave the EU, said: “Most of our workplace protections were introduced by the House of Commons before our membership of the EU or go further than the protections in other EU states. Britain has a very strong tradition of institutions in civil society social rights and providing a check on attempts to erode them.”

Anne Gulland, freelance journalist, London

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More articles online at bmj.com/brexit

Anne Gulland assesses how leaving the EU would affect working conditions.
Home run for integrated primary care?

The battle to remove barriers for patients needing quick, easy access to different types of care is being waged in primary care, where pilots are trying to crack the problem of integrated care, writes Adrian O’Dowd

Over the past few months, community workers, social care teams, and volunteers in the small Nottinghamshire town of Worksop have all started working under the same roof as general practitioners. Community workers have been given permanent space inside a general practice and arrangements are in place for social workers and volunteers to work there regularly.

The practice’s phone and wi-fi system has been upgraded to help these normally segregated services start to work together as a team with a single shared budget. This team is now building a closer relationship with local mental health services—it is hoped that mental health staff will also eventually work under the same roof—nursing homes, and hospitals.

“There is a huge amount we can do simply by improving communication and working together for patients,” says Steve Kell, a local GP who is leading the push for truly integrated care in the Larwood and Bawtry area, which includes Worksop. “I think it’s making a real difference.”

Kell, a former chair of NHS Clinical Commissioners, which represents commissioning groups nationally, says the new approach is all about providers working more closely with those who commission.

“Our three aims are to improve patient outcomes through more coordinated work, to improve staff wellbeing by making practices a better place to work and having a team based approach, and to create efficiencies for providers and commissioners,” he says.

It’s too early to say how the new approach is affecting outcomes or whether it is saving money. But one thing seems already clear—this is how local GPs want to work. The model is helping the practices with their recruitment of GPs and nurses.

Larwood and Bawtry is just one of 15 sites around the UK that has been working in this new way since 1 April, under a pilot scheme devised by National Association of Primary Care (NAPC) in collaboration with the NHS Confederation, and funded by NHS England.

More sites are expected to start testing the model—known as the primary care home model—later this year. They do not have to follow a specific formula but are being asked to come up with their own design, modelled on the population that they are serving, to shift away from the traditional isolated general practice model (see figure). Some, for example, are bringing different services under the same roof while others are improving the communication between services in different locations.

The NAPC’s chair, Nav Chana, says the new model promises to transform what primary care can offer patients, and NAPC president, James Kingsland, describes it as a “natural evolution.”

“A key facet of the primary care home model is balancing the

The model is based on patient populations of

30 000 to 50 000

personalled care— responding to the needs of an ill person—with looking at population health needs in a way that we have not done as a small single practice,” says Kingsland.

Currently, he explains, GPs broker a lot of work externally to services such as integrated foot care, incontinence, district nursing, musculoskeletal, or mental health services. But these teams are disconnected from first contact care and use different care records.

“We are working in one of the most fragmented systems I’ve ever seen. Most GPs are working in that isolated, traditional general practice environment. The primary care home model describes an organisation where the staff working within it have got a stake in that organisation.”

How it works

The model works like a multispecialty community provider and is based on patient populations of 30 000 to 50 000, with practices developing integrated staffing models as part of new ways of working and colocating care with community services, acute trusts, the voluntary sector, and social care.

Each site receives up to £50 000 from NHS England to support its set-up and have access to support and learning from the NAPC, the NHS Confederation, and NHS England’s new care models programme.

The pilots are not tied to a specific period and it is hoped they will carry on and be adapted after evaluation.

The idea is for clinical commissioning groups (CCGs) to devolve specific budgets to the test sites next year. Subject to agreement from CCGs, this would involve test sites having access to a whole population budget rather than simply transferring a lump of cash over to the sites.

The initiative is different to the NHS vanguards schemes, which are developing new care models, although it has some features in common.
The primary care home model’s focus, however, is on collaboration on a scale that is easy to handle. “We set the parameters of population at a very limited 30 000 to 50 000 size because we think that represents the optimum population size around which you can genuinely deliver care configured around the needs of population and community,” says Chana.

“Some of the sites are negotiating with their CCGs some parameters by which they will have access to the whole population budget, but some CCGs are trying to test this out with elements of the budget.”

Concerns have been raised about some aspects of the home model, such as the practicalities for some patients of travelling to a single site for treatment and the fact that some CCGs are not yet fully engaging with the model.

But Mike Holmes, clinical lead for the Royal College of General Practitioners supporting federations programme, says: “These are just things that need to be worked out.” There are also issues such as how the new model may affect medical indemnity cover that have yet to be resolved.

“If we are saying in this new model that people might be working in a slightly different way and taking on greater responsibility or working in different settings, their indemnity might change and as a consequence of that, the cost might be very different,” says Chana. “The indemnity organisations are not necessarily indemnifying people for these new models of care at the moment.”

Chana denies the accusation that the model is creating a new layer of bureaucracy under CCGs, saying: “It’s about provision and, effectively, it simplifies bureaucracy because if, in time, you have access to a whole population budget, then you don’t have to go through various committees and governing bodies and various approaches to do something that intuitively makes sense for the people you’re looking after.”

Inspiration to replicate the model
Almost 70 networks of GPs and health and social care staff submitted expressions of interest last year to become test sites, and some of those that were not selected have begun trying new approaches inspired by the primary care home model.

The Vale of York Clinical Network was formed after the area was not accepted as a test site for the primary care home model because its population was too big. The network of 30 general practices covering a population of around 300 000 has developed five or six community care hubs inspired by the same thinking.

“That sort of model is popping up all over the place, and people are beginning to realise that working at scale is probably the way forward,” says Holmes, who is also a member of the board of the Vale of York Clinical Network. He believes the primary care home model can work for large populations without becoming impersonal.

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“GPs are much more than gatekeepers”, p 358
BMJ CONFIDENTIAL

Simon Singh

Challenging pseudoscience

What was your earliest ambition?
I have a memory of standing next to the family record player, aged 8, telling my big sister that I was going to be a nuclear physicist. My PhD was in particle (sub-nuclear) physics, but then I morphed into a journalist.

Who has been your biggest inspiration?
James “The Amazing” Randi, a magician who became a father of the modern sceptic/rationalist movement. My writing career started by championing great science, but Randi made me realise that it’s equally important, perhaps even more so, to challenge pseudoscience.

What was the worst mistake in your career?
Avoiding computers when I was a teenager and developing a lifelong nervousness around technology.

What was your best career move?
Quitting physics after my PhD. I love physics and loved my PhD, but I could see colleagues who were brighter and quicker than I was.

Who is the person you would most like to thank, and why?
Mr Stephens, who taught me maths for seven years from age 11.

To whom would you most like to apologise?
Do internal organs count? I really should have done more to keep fit and healthy.

Where are or were you happiest?
Working on Tomorrow’s World and interviewing two of my heroes on the same day—Stephen Hawking and Garry Kasparov.

What single unheralded change has made the most difference in your field?
The advent of blogging and YouTube. Anyone can now sidestep the mainstream media and gain a following in a niche technical area.

Do you support doctor assisted suicide?
Yes.

What book should every doctor read?
The Demon Haunted World: Science as a Candle in the Dark, by Carl Sagan.

What is your most treasured possession?
An Enigma machine.

What, if anything, are you doing to reduce your carbon footprint?
Solar panels on the roof, smart thermostat, energy monitor, hybrid car, and a cork up my bum.

What personal ambition do you still have?
I’ve started a charity called Good Thinking. We challenge pseudoscience and promote good science. Also, I’m passionate about maths education, and Good Thinking is developing a pilot project due to start in two schools in September. If it’s successful and is adopted by every school in the country, I’ll die happy.

What is your pet hate?
It’s a tie between climate change numpties (such as Nigel Lawson), people who don’t realise that a firm handshake is a million times better than a hug or a kiss, and false balance in science journalism.

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