this week

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Judge queries GMC delay in sex case

A High Court judge has called for an independent review of the General Medical Council's delay in investigating a patient's sexual assault claim against a foundation year 1 doctor, which was thrown out by a medical practitioners tribunal nearly three years after the investigation opened.

Mr Justice Holgate made the call in a judgment quashing all the tribunal's findings against Michael Brookman, along with the decision to strike him off the UK medical register.

The tribunal rejected the patient's claim that Brookman had "touched her genitalia while undertaking a sexually motivated inappropriate examination" in October 2013. But it went on to strike Brookman off the register in February 2017 after finding him guilty of dishonesty in not immediately telling a locum agency and an NHS trust that were using his services about interim conditions placed on his registration.

He was also found to have been dishonest in not telling Swansea University, where he was applying for jobs as a lecturer, about a brief period of employment at Bournemouth University and about the reasons the conditions had been imposed.

The conditions, which included a ban on seeing female patients without a chaperone, had been put in place pending the outcome of the investigation into the allegations.

The GMC notified Brookman that it had opened an investigation into the case in April 2014. The tribunal hearing began in October 2016 but was heard in stages in October and December 2016 and February 2017, when the patient's allegations were finally rejected by the tribunal.

Holgate said, "First, I found it difficult to understand why it should have been necessary for some two and a half years to elapse before the hearing began in order to deal with the limited range of allegations in this case. Second, it was also difficult to understand why the weaknesses in the evidence of the patient and her husband could not have been identified during the investigation and a more realistic view taken of the chances of proving [the] allegations."

The judge said that the allegations were "of a very serious nature and needed to be resolved as soon as possible," as did those alleging a breach of the conditions. Further witness statements relating to essential factual aspects of the patient's allegations were not obtained until towards the end of 2015, and a statement from the ward matron in January 2016. A similar timescale

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Michael Brookman has been left in significant debt after being under suspicion for nearly three years before the sexual assualt claims were dismissed by the tribunal

LATEST ONLINE

- Hunt promises affordable homes and flexible hours to retain NHS staff
- Two thirds of Europe's psychiatric trainees are eager to migrate
- Managers agree temporary cover after ambulance service collapses

SEVEN DAYS IN

"Public should be consulted on vaginal mesh report"

A former member of the independent group set up by the Scottish government to review the safety and efficacy of transvaginal mesh implants has called for the final report to be put out for public consultation.

Consultant gynaecologist and obstetrician Wael Agur told a hearing of the Scottish Parliament's Public Petitions Committee on 28 September that the final report had not done enough to tackle the worries expressed in the group's interim report. Agur resigned from the review group four weeks before the final report was published in March this year.

The final report refused to recommend a ban of transvaginal mesh implants, to the dismay of hundreds of women who had complications after receiving the implants. Many of these women are taking legal action against the manufacturers.

While the final report acknowledged that many women had "life changing complications" following the surgery, it said that others had benefited from it.

Agur urged the committee to ask the government to open the final report to a public consultation period, of around six to eight weeks. He said similar procedures were adopted by the EU before the publication of its report on mesh.

Ingrid Torjesen, London Cite this as: *BMJ* 2017;359:j4570

Breast cancer

Women with disabilities miss out on screening

Women with disabilities are a third less likely to take part in breast cancer screening and a quarter less likely to take part in bowel cancer screening than women without a disability, said research published in the *British Journal of Cancer*. The study found that women with disabilities that affected eyesight, mobility, and their ability to self care were least likely to take part in screening.

Progress in outcomes is "stalling," charity warns

Falling uptake in screening, delayed treatment, and a shortage of diagnosticians are leading to a "worrying plateau in progress" in breast cancer outcomes, said the charity Breast Cancer Now. Its report highlighted that 72.1% of eligible women took up screening in 2015-16, down from 74.8% in 2005-06; that 93.5% of patients began treatment within 62 days of referral in the first quarter of 2017-18, down from 97% in 2011-12; and that 21% of breast radiologists were due to retire by 2020. It also said that too few postmenopuasal women with primary breast cancer were receiving bisphosphonates, despite evidence that the drugs could reduce the risk of breast cancer spreading to bone by 28%.

Epsom salts

Warning issued over liver damage

A 38 year old man developed serious liver damage after taking Epsom salts to treat gallstones, said doctors in the journal *BMJ Case Reports*. The man had lost his appetite and was jaundiced, and a biopsy specimen showed signs of liver damage. A naturopath had advised the patient to take three tablespoons of Epsom salts in lukewarm water. The man's liver function returned to normal six weeks after he stopped taking the salts.

Abortion

Ireland to vote on termination in 2018

The Irish government is to hold a referendum on relaxing its abortion law. Voters will be asked to decide on changing the Irish constitution, which allows abortion only if the mother's life is in danger. A woman convicted of abortion faces up to 14 years in jail, but women are allowed to travel abroad for termination. The referendum would take place in May or June, weeks before Pope Francis is due to visit the country.

Out-of-hours indemnity

£10m scheme will cover GPs fees over winter

NHS England has made £10m available for indemnity costs to help GPs working out-of-hours shifts from 1 October until Easter Monday 2018 to allow them to commit to more shifts without needing to negotiate changes to their indemnity cover. Doctors' leaders and providers of out-of-hours GP services have been warning about an impending winter crisis for months, because spiralling indemnity fees have meant that fewer doctors could afford to work. The BMA's Richard Vautrey welcomed the funding, but added, "GPs need a long term solution to the indemnity crisis, and this is something which the BMA is continuing to lobby the government on."

Medical errors

Apologising does not increase risk of lawsuits

Explaining and apologising to patients after a medical error does not result in a rise in lawsuits, a US study published in *Health Affairs* found. Researchers analysed 989 adverse events in cases that included an explanation of what happened, an apology, and offer of compensation where appropriate. Only 5.1% (47 of 929) led to claims or lawsuits, and 4%, including those referred because a claim had been made, were settled without lawsuits.

Court ruling

Boy with autism can have £100 a day drug

NHS England has agreed to fund a £100 a day drug for a 7 year old boy with autism and phenylketonuria after a High Court judge ruled its original refusal was "fundamentally flawed." Sapropterin dihydrochloride prevents protein accumulating in the blood of phenylketonuria patients, causing brain damage.

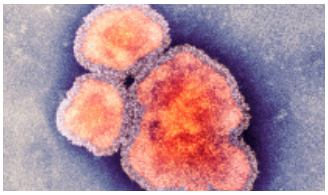
MEDICINE

Nobel prize

Unravellers of biological clock win medicine award

The 2017 Nobel prize for physiology or medicine, worth nine million Swedish krona (£830 000), has been awarded to three scientists for their work deciphering the molecular mechanisms controlling the body clock. In the 1980s, Jeffrey Hall and Michael Rosbash at Brandeis University, Massachusetts, and, separately, Michael Young at Rockefeller University, New York, isolated the genes relating to circadian rhythm in fruit flies. Hall and Rosbash then discovered that levels of the PER protein encoded by the period gene built up during the night and fell during daytime. Young found that the "timeless" gene he identified made a protein named TIM that is also needed for a normal circadian rhythm.

Measles



Disease officially no longer endemic in UK

The UK, Denmark, and Spain have eliminated endemic measles, meaning that 33 countries in WHO's European region are now free of the disease, having had no endemic transmission for at least 36 months. At the end of 2016, 42 of the 53 countries in the region had interrupted endemic transmission of measles for at least 12 months.

Delayed discharges

Longer hospital stays linked to rising mortality

Delayed discharges from hospitals are more common at times of higher mortality, a study published in the *Journal of Epidemiology and Community Health* has found. The number of deaths per month between August 2010 and March 2016 was compared with the cumulative number of days that acute care patients in England were late being discharged. The analysis indicated that for each additional day of late discharge the number of deaths increased by 0.39 (95% confidence interval 0.22 to 0.57). The findings for non-acute admissions were mixed. The researchers hypothesised that delays in discharge may postpone access to the right type of care.

Depression

Risk halved by an hour of exercise a week

The risk of developing depression was 44% lower in people who exercised for one or two hours a week than in people who had no regular physical activity, analysis of data on 22 564 people in the Norwegian Health Study has found. None had depression or anxiety at baseline, but 9-13 years later 7% of participants (1578) had developed clinically significant symptoms and 8.7% (1972) developed anxiety. The researchers, reporting in the *American Journal of Psychiatry*, calculated that 12% of the cases could have been prevented if people in the study had taken at least an hour of exercise a week.

Cite this as: *BMJ* 2017;359:j4563

HIV CASES

5164

new cases of HIV were reported in the UK in 2016, down 18% from

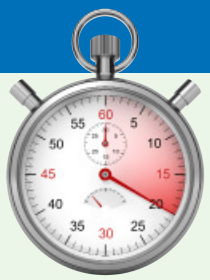
6286

in 2015. A 21% decline was seen among gay and bisexual men (from

3570

to 2810)

Public Health England



SIXTY SECONDS ON . . . NHS PROPERTY SERVICES

AREN'T THEY THE NHS LANDLORDS?

Yes, indeed. In April 2013, the Department of Health for England set up a limited company to take on the ownership and management of roughly 3600 NHS buildings and facilities, following the abolition of strategic health authorities and primary care trusts. Its portfolio includes around 1200 general practices, about 15% of the GP estate.

WHY IS IT A LIMITED COMPANY?

It's a fair question, one asked by our friends at the National Audit Office in a 2014 report that criticised ministers for not considering public ownership. The report admitted that a limited company had the advantages of commercial flexibility and possibility of a future sale.

SO, ARE WE TALKING RACHMAN?

Even a government agency could not stoop to the depths of the 60s slum landlord whose name is synonymous with unscrupulous exploitation. But NHS Property Services did raise GPs' rent and service charges in line with market valuation in April 2016, with some reporting rises from £15 000 to £80 000 a year. It has also removed subsidies on premises previously offered by primary care trusts, which has caused many general practices to be invoiced for the full cost of their occupation, perhaps for the first time.

BUT ISN'T THIS FAIR GAME?

The company argues it is and that a business-like approach is required to make the process more, well, business-like. In the old days many GPs' leases were operated without contracts, and subsidies offered varied wildly. NHS PS says it wants to remove such inconsistencies. Since it was set up the company has raised more than £203m from the disposal of 295 surplus properties, many of which, such as former Moreton-in-Marsh Hospital in Gloucestershire (below) were empty. Last year it reinvested £67m in upgrading and developing new facilities.

WHY IS IT THE BOGEYMAN THEN?

Removing subsidies has caused strife for practices that have historically factored them into running costs. The BMA has warned that the rigour with which costs are being pursued is threatening the viability of practices and has urged GPs to check the smallprint and negotiate before signing up to lease agreements.

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2017;359:j4561

CONTINUED FROM p 1

applied to the July 2014 allegations about the conditions.

"These are matters which ought to be reviewed independently for the MPTS [Medical Practitioners Tribunal Service], to see whether any delay was truly justified and, if not, whether these were merely isolated incidents," Holgate added.

His call came after two tribunal cases in the past month in which patients' allegations against doctors were held to be unreliable and the cases discontinued around three years after the initial complaint.

Holgate said that the tribunal had been "unjust" to go on hearing the case against Brookman, in which he was defending himself without a lawyer while taking an antidepressant, and should have adjourned for a health assessment.

The transcript of the tribunal hearing made it plain that Brookman was "having great difficulty in representing himself adequately," Holgate said. Brookman had said in evidence that the antidepressant made him treat as unimportant matters that were important.

The tribunal had been concerned about the drug's effect on him during the hearing and in the three preceding years and considered adjourning for psychiatric assessment. But counsel for the GMC argued that this was not needed, and the tribunal decided not to adjourn. Holgate said that he had reached the clear conclusion that this was "both wrong and unjust."

In addition, he said, in deciding to erase Brookman from the register, the most serious sanction available, the tribunal took into account only four points of mitigation. It excluded others that were material, such as the extent to which his behaviour was influenced by the stress of having to deal with the patient's allegations.

Brookman, 57, spent a long career as a science teacher before qualifying as a doctor in 2011. He has been left with a substantial debt and has had to enter an individual voluntary arrangement with his creditors.

A GMC spokesman said it would be reviewing the judgment carefully.

Clare Dyer, *The BMJ*

Cite this as: *BMJ* 2017;359:j4579

Number of British doctors working in Australia and New Zealand is rising

An increasing number of UK trained doctors are working in Australia and New Zealand, according to new registry figures. A total of 699 more doctors from the UK were registered to practise in Australia in 2016 than in 2014, a 17% rise, show data from the Australian Health Practitioner Regulation Agency (table 1).

Over the same period the number of UK doctors who were registered to practise in New Zealand also rose by 17% (from 424 to 497), but the number of UK trained doctors who were registered to work in the US was 1.4% lower in 2016 than in 2014.

In July 2017, a total of 232 708 doctors were registered with the General Medical Council to practise.

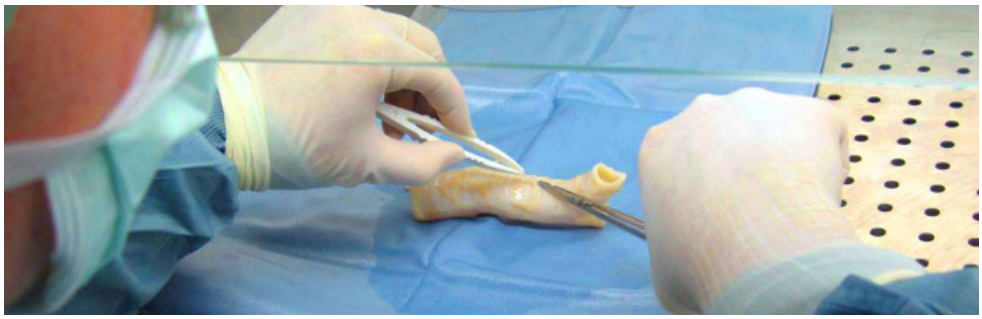
Concern arose during the junior doctor contract dispute in England in 2015 and 2016 that many would leave the NHS. A survey conducted in October 2015 of 4150 junior doctors found that nearly three quarters (72%) said that they planned to leave the NHS if the government imposed a contract in August 2016.

Doctors who wish to practise abroad often need a certificate of current professional status (CCPS) (also known as a certificate of good standing) from the GMC, a document that enables them to register with an overseas regulatory body or employer.

The GMC said that between mid-September 2015 and mid-February 2016 it saw a large increase in the number of CCPS applications after junior doctors used it as a way to protest against proposed contract changes (Table 2). But it said that it could not distinguish between doctors making a protest application and those actually considering working abroad.

Not all doctors who request a certificate go on to leave the UK. Despite the peak in applications in 2015, the proportion of doctors issued with certificates who remained

The GMC can't distinguish between doctors making protest applications and those who are actually considering working abroad



Artificial implants lab breached safety rules

Wigmore report finds a catalogue of errors at University College London

Artificial implants produced at University College London and used on patients abroad were in breach of manufacturing regulations and had not been properly tested in animals, an independent inquiry has found.

Stephen Wigmore, professor of transplantation surgery at Edinburgh University found a catalogue of errors at UCL, where windpipes, arteries, and tear ducts made from polymer were supplied by a laboratory that was not licensed to make clinical grade devices. This breach should be reported to the Medicines and Healthcare Products Regulatory Agency "as soon as possible," the report concluded.

The artificial organs were made of a polyurethane modified to imitate natural materials. Before implantation the plastic scaffolds were clothed in cells taken from the patient. The Wellcome Trust had awarded grants for the development of these materials by Alexander Seifalian and others at UCL who had close ties to Paolo Macchiarini,

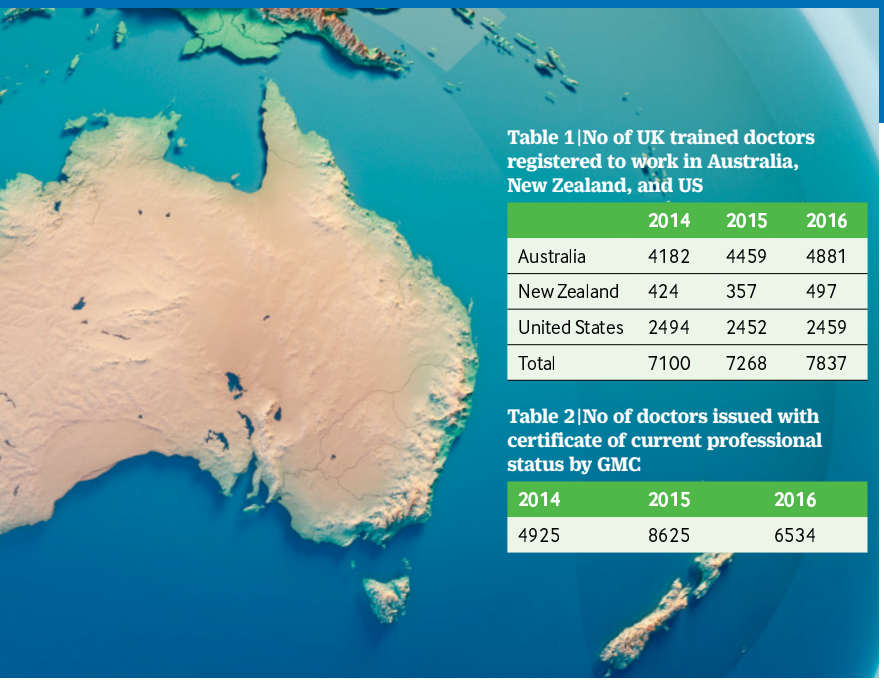


Table 1 | No of UK trained doctors registered to work in Australia, New Zealand, and US

	2014	2015	2016
Australia	4182	4459	4881
New Zealand	424	357	497
United States	2494	2452	2459
Total	7100	7268	7837

Table 2 | No of doctors issued with certificate of current professional status by GMC

2014	2015	2016
4925	8625	6534

registered with the GMC was similarly high across the period. Of the doctors who were issued with a CCPS in 2014, 86% (4362) remain licensed with the GMC, as do 94% (8106) of those issued with a CCPS in 2015 and 94% (6143) of those issued with a CCPS in 2016.

Jeeves Wijesuriya, chair of the BMA Junior Doctors Committee, said that the figures would come as no surprise to those working in the "overstretched, under-resourced NHS."

He said, "We can't underestimate the impact that working under constant and extreme pressure has on the morale and wellbeing of our workforce, which can lead to doctors taking extended time off to recover from stress and burnout or leave the NHS altogether.

"We need an urgent plan from the government to address the workload, workforce, and funding issues facing the NHS, otherwise these numbers will only continue to rise, undermining the NHS's ability to meet rising demand on service and leaving those left in the NHS working under even more pressure."

Abi Rimmer, *The BMJ*

Cite this as: *BMJ* 2017;359:j4554

the charismatic but now discredited surgeon who worked at the Karolinska Institute in Stockholm.

In 2011, Macchiarini asked Seifalian to produce an artificial trachea for an Eritrean man, then living in Iceland, who had cancer of the trachea. Seifalian deputed the task to Claire Crowley, a first year doctoral student, without seeking approval for making a clinical grade product in premises not licensed to do so. Two tracheas were made, seeded with the patient's cells and implanted. Macchiarini declared the operation a success, but in reality the implant failed, and the patient died. A second operation, in Florence on a 19 year old British woman with tracheal cancer, was also a failure.

In a further case a 26 year old drug user in Tehran with a failing femoral artery received a graft to bypass the artery. George Hamilton, professor of vascular surgery at UCL, told the inquiry that this was negligent as the implant would inevitably become infected and would need to be removed, with the loss of the limb or life. No outcome has been reported.

Wigmore told *The BMJ* it was essential for biomaterial or regenerative medicine researchers to fully understand the rules. "These regulations are designed to ensure quality and safety and ultimately to protect patients," he said.

His report details a series of complaints made against Seifalian in 2015. There were long delays in dealing with these allegations, but in 2016, he was dismissed by UCL after a tribunal found him guilty of financial misconduct. He faces two more research misconduct inquiries.

Seifalian, who now runs a company called Nanoregmed, did not respond to an inquiry from *The BMJ*. But he told the *Guardian* that he was being made a scapegoat for activities in which many people had been involved.

Nigel Hawkes, London

Cite this as: *BMJ* 2017;359:j4572

Suspension for diabetes editor who faked data

A former editor of the *British Journal of Diabetes* who was found last April to have fabricated research data and forged the signatures of coauthors has been suspended from the UK medical register for four months.

Paul Grant had been due to take up the post of editor in chief of *Clinical Medicine*, the journal of the Royal College of Physicians, when allegations surfaced of irregularities in five research papers he submitted. He never took up the post.

Two of the papers were published and later retracted. The most serious allegations concerned a study of anxiety and depression in 350 patients with type 1 diabetes who received insulin pump therapy at King's College Hospital in London. Lacking complete age data for his cohort, Grant fabricated these and also the prevalence of psychiatric morbidity, a medical practitioners tribunal found. He also named coauthors without their approval, forged colleagues' signatures, and failed to notify real coauthors of changes and manuscript submissions he had made, the tribunal found.

The GMC asked for Grant's registration to be suspended but made no recommendations as to its length. His counsel asked for conditions to be imposed on his registration, or a suspension of less than three months, noting that he had made no financial gain and harmed no patients. The tribunal heard testimonials from colleagues and patients at a diabetes programme in Sussex, where Grant now works.

Clare Dyer, *The BMJ*

Cite this as: *BMJ* 2017;358:j4537

Cardiologist cleared of sexual assault

A consultant cardiologist has been cleared of sexually assaulting three women during medical examinations at Lewisham Hospital in southeast London. Sumit Basu, 59, was acquitted at Woolwich Crown Court of seven charges of sexual assault and three charges of assault by penetration between 2006 and 2014.

Allegations were first made to police in March 2016 by a second year medical student, who claimed that Basu touched her breasts on the first appointment and on the fourth appointment inserted his gloved fingers into her vagina. The two other women came forward after media coverage of his arrest.

Basu, who qualified in India in 1983, told the jury he was "absolutely devastated" by the accusations. He accepted that rectal examinations were rare in cardiology clinics but told jurors, "You have to have a feel. You have to be a whole doctor."

Interim conditions were imposed on his medical registration in May 2016, including a ban on consultations with female patients without a chaperone. His registration was suspended in March 2017.

Clare Dyer, *The BMJ*

Cite this as: *BMJ* 2017;358:j4533

Figures show big increase in outstanding premises fees for some tenant GPs

"If practices sign up to unwise lease agreements it could jeopardise their viability"
Ian Hume

General practices in England owe more than £90m to NHS Property Services in outstanding premises fees, official figures have shown.

The figures were disclosed in parliament by the health minister Philip Dunne in response to a request from Labour's shadow health minister Justin Madders. They show that the total costs charged to GP tenants that remain outstanding were £9m in 2014-15, £28m in 2015-16, and £55m in 2016-17.

The disclosure came as talks continued between the BMA and NHS Property Services to resolve the ongoing dispute over substantial increases that the agency had applied to GPs' rent and service charges.

NHS Property Services is a limited company owned by the Department of Health for England. It took over the leases for general practices in rented premises in April 2013 after primary care trusts were abolished. In 2015 it began removing premises subsidies previously offered by PCTs, which has resulted in many general practices being invoiced for the full cost of their occupation for the first time. It also put GPs' rent and service charges in line with market valuation in April 2016, which has led to large increases for some.

NHS Property Services said that its changes were justified because many general practice leases had previously been operated without contracts and PCTs had been inconsistent in the levels of subsidy they offered. It also argued that the move to market rents would improve practices' understanding of the true cost of occupation and incentivise them to make efficient use of space.

Although market rent is reimbursed by primary care commissioners and does not affect practices directly, GPs' leaders have said that the removal of subsidies has seen some practices' lease charges soar from £15 000 to £80 000 a year.

The BMA has urged practices not to sign lease agreements that threaten their viability, emphasising that terms set by NHS Property Services are negotiable on an individual practice basis and are not enforceable. It has argued that GPs have been given insufficient clarity about why and how charges have changed and that NHS Property Services has employed "underhand tactics" in getting practices to sign lease agreements.

Limits on working hours may be relaxed after Brexit

Legal protections ensuring that doctors do not breach limits on safe working hours could be eroded after the UK leaves the European Union, an employment expert has warned.

Jason Heyes, professor of employment relations at Sheffield University, told a meeting discussing Brexit's effect on healthcare that the EU's working time regulations, which ensure that doctors do not work for more than an average of 48 hours a week and guarantee rights such as rest breaks and holidays, might be targeted by a Conservative government when the UK leaves the EU.

"Once UK policymakers have the ability to start tinkering with working time regulations they will start doing so," he told the meeting, run by the Royal Society of Medicine's trainees' section.

He later told *The BMJ* that ever since the working time directive was incorporated into UK law in 1998 it had been a Tory target. "For many years the Conservative Party has been critical of the working time regulations, and the right wing of the party has been implacably opposed to them," he said.

The Conservatives' criticism is shared by some royal medical colleges, which believe that the regulations restrict the amount of time available for training of doctors. Doctors can opt out of the 48 hour limit, and a Royal College of Surgeons review of the regulations called for more widespread use of this. The UK is one of the few EU countries to use the opt out.

"We cannot allow the regulations to be eroded in any way. The results would be catastrophic"
Jeeves Wijesuriya

Heyes said that opposition from the government and from some within the NHS could weaken the rules. "My suspicion is that once they are no longer obliged to respect EU labour laws, and particularly given the resource constraint in the NHS, the working time regulations are going to be something that the government looks at," he said.

However, Jeeves Wijesuriya, chair of the BMA's Junior Doctors Committee, told the meeting that the BMA would oppose any attempt to water down employment protections. "We cannot allow the working time regulations to be eroded in any way, shape, or form for our workforce, because the results would be catastrophic," he said.

"If we do not have limits on hours and protected rest periods after long on-calls, it's not just doctors who will be at risk but the patients we care for."

Anne Gulland, London

Cite this as: *BMJ* 2017;359:j4547

Ian Hume, lead on premises for the BMA's General Practitioners Committee, said, "NHS PS are trying to pass on all the costs to their tenants, many of whom don't have leases in place. But we must make sure that practices understand their liability, and it must be fair and reasonably charged.

"We are concerned about the risk to the sustainability of some practices. If they sign up to unwise lease agreements it could jeopardise their viability."

Hume said that the BMA was still negotiating with NHS Property Services to resolve the dispute. He said that one option might be to put a cap on service charges to limit GPs' liability. "This would enable practices to have confidence to sign up to leases," he said.

A spokesperson for NHS Property Services said, "Most of the increase in the amount invoiced and outstanding will be due to the move to market rent, which was introduced to help improve understanding of the true cost of occupation.

"We are continuing our discussions with individual practices to resolve queries and encourage payment of outstanding amounts. It is important that bills are paid so that we can continue to reinvest in the NHS estate. Last year we invested £67m to upgrade and develop new facilities across England."

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2017;358:j4529

MALCOLM WILLETT

PARTY CONFERENCE REPORT

Labour appears to be watering down its vow to abolish PFI

High on its surprise performance in the general election, Jeremy Corbyn's Labour Party headed to its annual conference in Brighton last week in buoyant mood.

Though there was not a huge push on NHS issues (save for shadow health secretary Jonathan Ashworth's call for an extra £500m to ease winter pressures), two potentially important themes emerged.

The first was on public service funding and the private finance initiative (PFI). Shadow chancellor John McDonnell used his speech to promise that "based on our fiscal credibility rule…to pay for our public services, we will close the tax loopholes and avoidance scams used by the mega-rich, and we will make sure the rich and the giant corporations pay their way."

McDonnell said, "There will be no new PFI deals signed by us…I can tell you today, it's what you've been calling for. We'll bring existing PFI contracts back in-house."

That could prove expensive. The government's most recent projections of the outstanding cost of PFI in the NHS show that in 2016-17 the NHS in England paid an estimated £2bn for 105 past and current PFI projects, some of which run to 2050.

However, in interviews Ashworth downplayed McDonnell's PFI promise, telling BBC Radio 4's *Today* programme that "NHS experts generally accept that it's only a handful which are causing hospital trusts across the country a significant problem, but let's look at every single one in detail."

Ashworth's commitment to another PFI review (to follow those of the Treasury select committee, the health select committee, and the Office for Budget Responsibility, plus several studies by the National Audit Office) is unlikely to turn up many bad PFI contracts in the NHS that are currently not on the radar. It is, however, an interestingly reality based move away from the McDonnell position.

If a Labour government is formed, and if Brexit has caused the economic damage that is widely predicted, then any infrastructure spending that can be funded from taxation alone may simply not meet the actual or perceived need.

Deselecting GPs

Another story in the margins of the conference was spotted by the *Guardian*'s live blogger Andrew Sparrow, in a section on making public services more accountable.

Corbyn told the conference, "The kind of democracy we should be aiming for is one where people have a continuing say in how society is run, how their workplace is run, how their local schools or hospitals are run. That means increasing public accountability and democratisation of local services."

"IT'S ONLY A HANDFUL OF CONTRACTS WHICH ARE CAUSING HOSPITAL TRUSTS A SIGNIFICANT PROBLEM"
Jonathan Ashworth, left, downplaying John McDonnell's PFI pledge

Sparrow reported that "one idea being kicked around informally by Labour MPs would be to enable patients to somehow vote out GPs if they feel they are getting a bad service."

Clearly, this is not official party policy. But so many aspects of this idea are bad, it's hard to know where to start. In the first place, there is a significant shortage of GPs: NHS England reckons at least 5000. So, alternative providers who could take over from an unsatisfactory incumbent don't actually exist. Then there is the issue of the premises, which most GPs working under GMS contracts tend to own. It wouldn't be possible for a future Labour government to pursue this policy without expropriating massive amounts of private property. That would be highly expensive in compensation and open to vigorous legal challenge.

Were the local community to be offered the chance to deselect its GPs, would the criteria the public use be sensible ones? What would be the fate of a general practice that had a robust policy on antibiotic prescribing? Would we go full-on reality television and have a weekly diagnose-off between the bottom two practices?

Andy Cowper, editor Health Policy Insight

Cite this as: *BMJ* 2017;359:j4545

THE BIG PICTURE

NHS staff march against ID checks

Healthcare professionals and supporters took to the streets in London, Manchester, and Newcastle on 30 September to raise awareness about the charges being introduced in the NHS, often for the most vulnerable patients, such as refugees.

The protest was organised by the group Docs Not Cops (#patientsnotpassports) in collaboration with Medact Refugee Solidarity Group, Sisters Uncut, and Migrants Organise.

In February, England's health secretary, Jeremy Hunt, announced that all patients who accessed NHS services would have their identification checked and that people who did not qualify for free care would be charged upfront. The changes are being piloted in more than 20 hospitals and will be rolled out nationally on 23 October.

Timesh Pillay, a core medical trainee in west London, described the policy as a "scattergun" approach, with people with foreign sounding names being targeted. Pillay said that he had seen patients being visited on wards by Home Office staff, against official rules, and seen documentation in notes demanding that care be withdrawn because patients were unable to pay. "I have even heard of people who have asylum cases pending being told that they are not entitled to NHS care and that not paying could affect their case," he said.

The new policy was inappropriate in a country that had reaped the benefits of overseas trained staff and at a time when many countries were trying to establish universal healthcare, said Pillay.

"My motivation [for getting involved in Docs Not Cops] comes from the fact that the NHS is a leader worldwide and it is built on the foundation of resources from around the world. That it is broadly paid for by British taxpayers is false. It feels inequitable to me," he told *The BMJ*.

Zosia Kmietowicz, *The BMJ*

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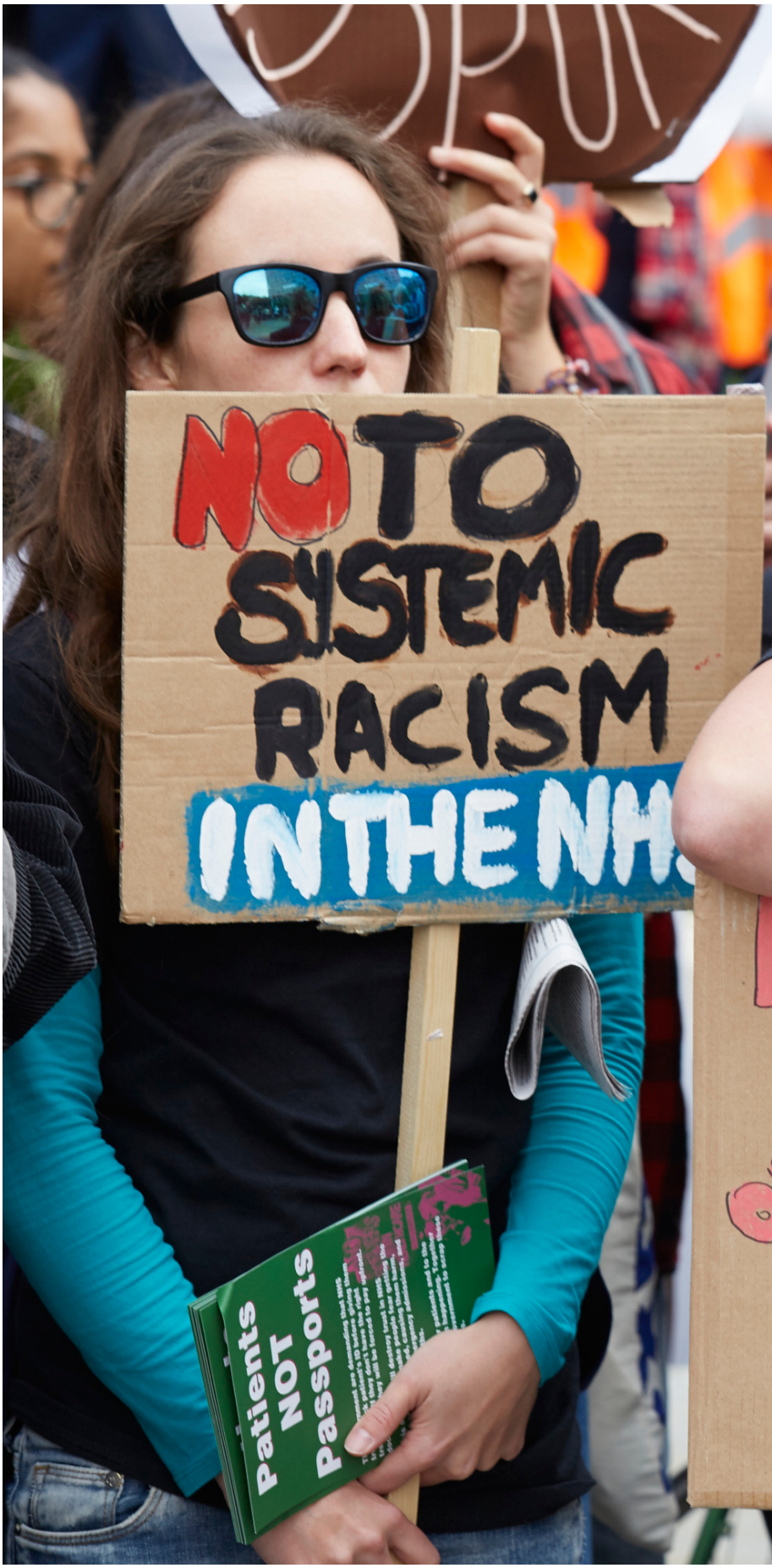

CLAUDIA MORONI

EDITORIAL

Threat to health from environmental plastics

It's time to pull our heads from the sand and properly research safe thresholds

Globally, an estimated 8.3 billion tonnes of plastic have been manufactured since mass production began in the 1950s. Eighty per cent of this astonishing mass has accumulated in land fill or the natural environment.[1] When degrading, plastic products release microplastics—tiny (<5 mm) particles and fibres —which contaminate the marine environment.

More recently, their presence in dietary components and the air we breathe has been reported, prompting speculation about risks to public health.[2]

Inspired by a lack of data on the contamination of drinking water by microplastics, the multimedia outlet Orb conducted an exploratory study with the University of Minnesota's School of Public Health to test 159 tap water samples from seven countries.[3] Eighty three per cent of the tested samples were contaminated with microplastics.

The water samples contained up to 57 microplastic particles per litre, with average global concentrations of 4.34/L. The authors estimate that we may consume 3000 to 4000 microplastic particles each year from tap water alone.[3]

Should we be worried? These numbers are relatively low compared with other sources of particulate pollution such as urban traffic and subway emissions.[14] However, this is an emerging area of research. Only a fraction of dietary components—shellfish, salt, honey, sugar, beer, tap water—have been tested, and our understanding of plastic contamination of the air we breathe is limited. Furthermore, detecting and identifying microplastics is a technological challenge. Reported concentrations are probably underestimates.

Although no definitive studies on health effects have been conducted, there are several mechanisms through which harm could occur—for example, by triggering inflammation.[5 6] Environmental microplastics also carry a cocktail of chemicals, including additives that are incorporated during manufacture[7] and accumulated contaminants from the surrounding environment.[8] These contaminants often have known reproductive, carcinogenic, and mutagenic effects.

Occupational hazard

The risk from chronic occupational exposure to microplastics and their subsequent accumulation in the body is real. People working in the textile industry have been shown to develop lung disease after chronic airway exposure to nylon flock.[10] Similar symptoms have been reported among workers in plants making polyethylene and polypropylene flock.[11 12]

Orb's investigators did not conduct chemical analyses to confirm the fragments were actually plastic, so their results should be interpreted with caution. The lower size limit of detection was 100 µm, and although microplastics in this size range are unlikely to cross the gut wall after ingestion in drinking water, this study does not rule out the presence of smaller, more bioavailable microplastics in the analysed samples, along with any associated harmful contaminants.

The authors estimate that we may consume 3000 to 4000 microplastic particles each year from tap water alone

EPA/REX/SHUTTERSTOCK

A scavenger collects plastic in Ciliwung River in Jakarta, Indonesia

Before considering measures to protect public health, it is essential to understand the sources of microplastic contamination that can enter the body. One option to reduce ingestion through tap water is to improve the efficiency of filtration. But the composition of any new devices must be carefully considered since plastic based filters may simply add to the contamination. Initiatives such as the UK's introduction of a charge for plastic bags and the ban on plastic microbeads in personal care products, which will be implemented by 2018, are primarily focused on the preservation of marine life, not human health.

The investigation by Orb is far from comprehensive, but it highlights an urgent need for bigger, better, and more definitive studies. We need to establish the toxic characteristics of microplastics, their behaviour in the body, and what constitutes a safe threshold for exposure when plastics are either ingested or inhaled. We must also relate these data to the different sources, types of plastic, and concentrations we are currently exposed to and, importantly, will be exposed to in the future thanks to the growing global addiction to plastic in all its forms.

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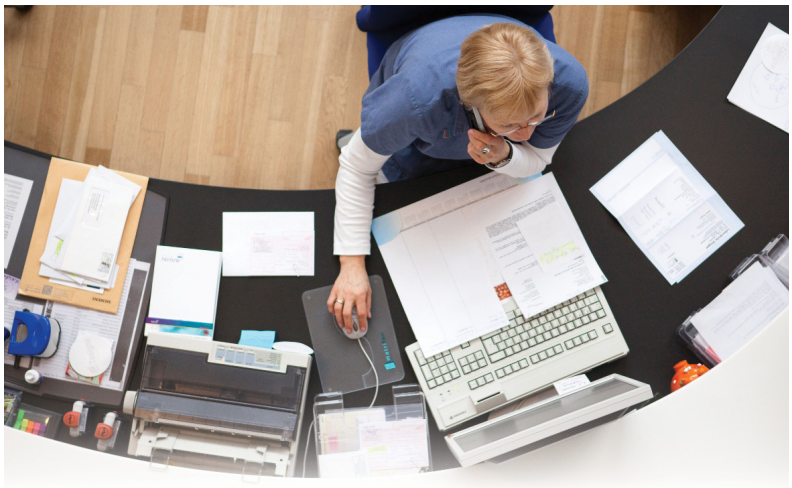
Rights and duties when general practices close

Where can patients go? Do local surgeries have to accept those displaced? As events in Folkestone show, losing GPs is an increasingly common—and fractious—scenario. **Gareth Iacobucci** reports



ALAMY

Receptionists in remaining practices struggle to cope with the influx of patients

Why are we talking about practice closures?
The ongoing issue hit the headlines again at the end of September when, after being asked to accept patients from a neighbouring practice that closed, a group of GPs in Folkestone had their request to formally close their seven practice lists rejected.

How big an issue is closure?
In 2016-17, 202 GP surgeries in England closed or merged, a record number and a 120% rise from 92 a year earlier. Around 265 000 patients had to change practice in 2016, up 150% on 2014. Folkestone, which has reported a shortage of 16 full time equivalent GPs, is not an isolated example. Seven practices in Brighton and Hove have closed since February 2015, with an eighth due to shut at the end of this month. An estimated 33 500 patients in the city have had to change GP since 2015.

Why is it happening?
A perfect storm of factors, according to the BMA, whose chair, Chaand Nagpaul, says, "Practices are facing this dire situation because they are being overwhelmed by rising patient demand, cuts to funding, staff shortages, and more unfunded work being moved from hospitals into the community."

What is the usual process for a closure?
A practice triggers its closure by handing its contract back to the commissioner (NHS England or the local clinical commissioning group). The commissioner is responsible for informing patients that they need to find an alternative practice to register with, subject to capacity at the other practices.

What are patients' rights?
All UK residents have a legal right to choose and register at a general practice if they live within that practice's boundary area. If a practice closes, patients have a legal right to transfer to any practice within a specified radius, which varies depending on the provision of surgeries. For example, South Tees Clinical Commissioning Group in April 2017 suggested alternatives within a 6 mile (9.6 km) radius; Kingston CCG in May 2016 suggested practices within 1.5 miles.

How long do patients have to re-register?
There are no national rules stipulating how much time patients should be given. Commissioners typically write to patients around 2-3 months before a practice closes, giving them this period to register elsewhere.

Are practices obliged to register patients?
Government regulations state that practices must accept patients who apply to register unless there are "reasonable grounds" to refuse. Such grounds would include where patients live outside the practice boundary; where it would be more appropriate, because of a patient's particular circumstances or clinical need, to register with a practice closer to home; or where the practice has no capacity for new patients. Even in these cases NHS England can assign patients to a practice whose list is not formally closed.

What is formal list closure?
A practice can apply to formally close its list if it believes that its workload is jeopardising its ability to provide safe care to its patients. If NHS England or a local assessment panel approves the request, having considered the potential effects on patients and neighbouring practices, a practice can close its list for at least three months but less than 12 months.

What if local practices don't have capacity?
The CCG has a legal responsibility to ensure patients can register with a GP. If practices don't have capacity to take on displaced patients, commissioners could advise them to register further afield—but there is little precedent for this. South Kent Coast CCG argued that it had "no choice" but to reject the request from the seven Folkestone practices to formally close their lists, because of the negative impact that multiple list closures would have on the town.

How can practice closures be prevented?
The BMA has consistently argued for more resources to support struggling practices and stem the number of practice closures.

NHS England envisages that small and singlehanded practices will increasingly be replaced by super-partnerships and federations of local practices, but many GPs think that its *General Practice Forward View* plan has failed to deliver on its promise to provide immediate relief to frontline services.

Last month the BMA revealed that more than half (54%) of GPs balloted would consider temporarily suspending patient registration in response to the workload crisis, and 44% said that they would consider applying for formal list closure. The BMA will not be making a decision on holding a formal ballot for industrial action at this stage, but it will use its survey results "to support negotiations and to call on the government to deal with the current crisis with far greater urgency."

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CANCER DRUGS EDITORIAL

Do cancer drugs improve survival or quality of life?

You don't need to know, according to our broken regulatory system

When in the lifecycle of a cancer drug should an improvement in survival or quality of life be demonstrated? Some argue the benefits should be evident before marketing. Others, me included, believe that for some indications, a drug might receive provisional approval based on surrogate outcomes, with overall survival or quality of life assessed after market authorisation. The one answer that seems unjustifiable is never. And yet, this is often what happens, according to two recent studies.

The first found that between 2008 and 2012 the US Food and Drug Administration (FDA) approved most uses of cancer drugs without evidence of survival or improved quality of life (67%, 36/54). Among the approvals, only five (14%) were shown later to improve survival.

The linked paper by Davis and colleagues (p 17) extends these findings.[2] In their study of cancer drugs approved by the European Medicines Agency (EMA), 57% (39/68) had no supporting better survival or quality of life evidence when they entered the market. After a median of 5.9 years on the market, just six of the 39 (15%) had been shown to improve survival or quality of life.

Minimal benefit

Three further facts help characterise the regulatory climate. First, when drugs do offer survival advantages, the gains are often marginal. Of the 23 drugs that improved survival in the new study, 11 (48%) failed to meet the modest definition of "clinically meaningful benefit" set by the European Society of Medical Oncology.

Second, the small benefits typically occur in trials conducted in unrepresentative patient populations—younger and with less comorbidity than average clinical populations. When a marginal drug advantage is applied to a real world population, a small benefit may vanish because of the fine balance between risks and benefits typical of these agents.

Finally, many of the surrogate outcomes used for approval are poorly correlated with survival.[6] For others, the strength of the correlation is untested. This is true for the FDA's regular approval pathway as well as the accelerated approval route. Notably, regular approvals are not usually coupled to post-marketing requirements for further trials. This means the surrogate outcome, often unvalidated, may be all we ever have.

These facts paint a sobering picture. Add in the average cancer drug costs — in excess of $100 000 (£75 000) per year of treatment—and the conclusion seems to be that the regulatory system is broken.

Huge expenditures

In the US, this means huge expenditures on cancer drugs with certain toxicity but uncertain benefit. The US Medicare programme is legally required to pay for any drug approved by the FDA without negotiation on price.

In Europe, agencies such as NICE exclude from reimbursement drugs that provide only marginal or uncertain benefits at high cost. However, it is only because regulators are lax that payers have had to wield the stick.

What can be done? The default path to market for all cancer drugs should include rigorous testing against the best standard of care in randomised trials powered to rule in or rule out a clinically meaningful difference in patient centred outcomes in a representative population. Deviations should be the exception. When surrogates are used, post-marketing studies with clinically meaningful and patient centred outcomes must be completed and published. Patient level data should be shared.

Health technology assessment programmes should reject modelled measurements of survival, which are unreliable and may unintentionally incentivise the industry not to conduct trials that evaluate survival directly.

We have an obligation to expose patients to expensive and toxic treatment only when they can reasonably expect an improvement in survival or quality of life. These studies suggest we may be falling far short of this benchmark.

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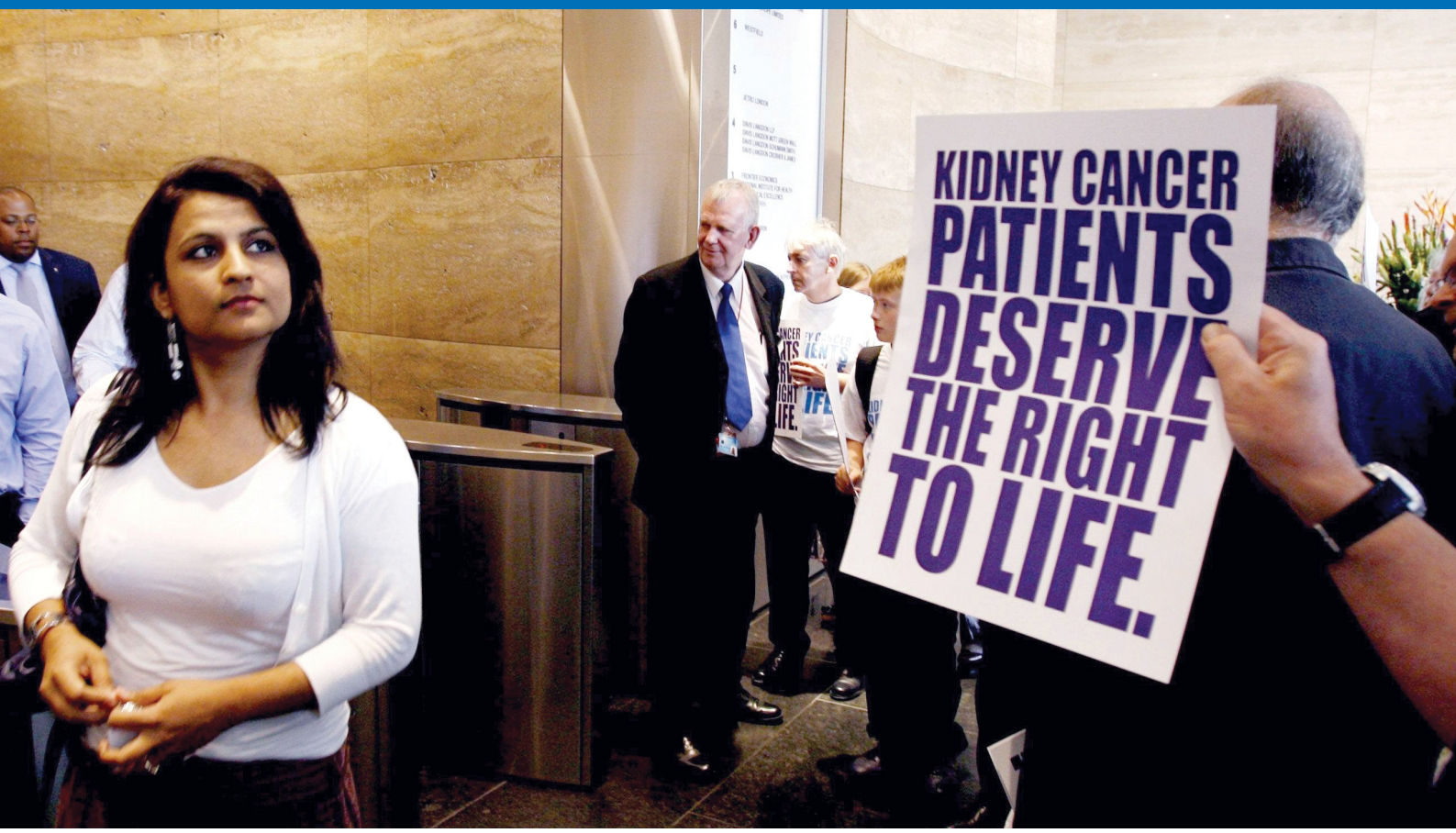
DRUG REGULATION

High on price, short on evidence

A study published in *The BMJ* this week shows how most new cancer drugs are failing to deliver any clinically meaningful benefit. It's time for Europe to raise the evidence bar before market approval, finds **Deborah Cohen**



Most cancer drugs entering the European market do so without clear evidence of extending or improving quality of life, new research published in *The BMJ* has found.

The findings raise serious questions about why the current regulatory environment supports the approval of cancer drugs that may leave patients at risk of toxicity and reduced quality of life without deriving meaningful benefit.

Out of the 68 cancer drug indications approved by the European Medicines Agency during 2009-13, 57% (39) entered the market without evidence of a survival or quality of life benefit. Even when the drugs did show survival gains over existing treatments, these were often marginal, researchers found.

Many of the drugs were approved on the basis of surrogate endpoints despite evidence that these are not a reliable indicator of overall survival or quality of life for most cancer treatments.

"When expensive drugs that lack clinically meaningful benefits are approved and reimbursed within publicly funded healthcare systems, individual patients may be harmed, important resources wasted, and the delivery of equitable and affordable care is undermined," the researchers say.

The study comes at a time when European governments are starting seriously to challenge the high cost of drugs. While it's hard to know how much healthcare systems are paying for cancer drugs because prices are often negotiated behind closed doors, the total amount spent on cancer care is growing, partly because of the cost of drugs.

Inadequate evidence

The research found that the EMA is basing many approval decisions on uncontrolled study designs or surrogate endpoints, which don't always translate into outcomes which make a difference to patients.

Some of the cancer drugs were given "conditional marketing authorisations," on the understanding that postmarketing studies would assess overall survival or quality of life. If the drugs are subsequently found to be clinically ineffective or unsafe, then the EMA can withdraw them. The study in *The BMJ* identifies 10 drugs approved under these fast track arrangements, but after four years of market entry none of them had good evidence that they either extended or improved life for patients.

The fact that so many of the new drugs on the market lack good evidence that they improve patient outcomes puts governments in a difficult position when it comes to deciding which treatments to fund.

In 2016, European health ministers issued a statement saying that new medical products "pose challenges to individual patients and public health systems in particular regarding their added value." This, they said, affects patient access, affordability, and the financial sustainability of health systems.

As an example of the pressures put on health systems, a recent Bristol-Myers Squibb

Headline making campaigns, such as the one mounted by patients in 2008 outside the London HQ of NICE (above), put pressure on regulators to authorise new drugs that lack clear evidence of efficacy

funded analysis compared licensed drugs for six different cancers across Europe and Canada and concluded that reimbursement decisions seem inconsistent. In an accompanying press release, the authors of the analysis stated: "There are potentially 200 000 patients in 12 countries who by licence should have access to drugs but are not getting them because of the reimbursement decision."

Their underlying premise was that the EMA grants licences to "safe, effective cancer treatments where access to the drug can improve and prolong life" and these drugs should be paid for.

In the eyes of the industry the problem is with national reimbursement, yet the overwhelming picture now, from not only *The BMJ* study but from studies published in *Lancet Oncology* and elsewhere, is that cancer medicines are being licensed that do not deliver clinically meaningful benefit.

The BMJ has found methodological problems with trials that EMA has either failed to identify or overlooked (box, right). This includes the trials' design, conduct, analysis, and reporting.

Such flawed clinical trials can lead to bias and further difficulties in identifying the true effectiveness. Unless there's thorough scrutiny of this regulatory evidence after approval, governments may make poor decisions about how to prioritise health budgets.

Unrealistic expectations

Perhaps most importantly, however, the fact the drugs have been given the imprimatur of regulatory approval may cause patients and doctors to have unrealistic expectations about their benefits and harms.

According to Richard Sullivan, professor of cancer and global health at King's College London and director of the Institute of Cancer Policy, doctors cannot be expected to be gatekeepers. In many cases new cancer medicines with low clinically meaningful benefit continue to be prescribed. "They may inappropriately script cancer drugs because of patient and family pressure; a lack of understanding of how new complex therapies work; or because of the culture of medical oncology in the absence of multidisciplinary decision making," he says. "If patients are not offered alternative modalities, including palliative care, in end-of-life settings then the risk of inappropriate or futile treatment with chemotherapy and immunotherapy increases."

Sullivan says the processes that allow a drug to be funded in national health services across Europe vary in their robustness and due diligence around judging clinical evidence. Some health technology assessment bodies view themselves as secondary gatekeepers to stop use of drugs that the EMA has licensed without evidence of benefit.

The Tories used access to new drugs as a key plank in their 2010 campaign

EMA'S DUBIOUS PRACTICES

Lenience on trial design

Approval of **mifamurtide** in 2009 for non-metastatic osteosarcoma was based on a pivotal trial that was not designed to evaluate clinical efficacy. Instead, the factorial design trial was aimed at evaluating the effect of mifamurtide and another agent, ifosfamide. In 2007, the FDA's oncologic drugs advisory committee raised serious concerns about the study design and choice of comparators. It concluded mifamurtide failed to show substantial evidence of efficacy.

Pomalidomide was approved in 2013 for relapsed or refractory multiple myeloma. The trial supporting this indication compared patients who were randomly allocated to receive pomalidomide in combination with low dose dexamethasone with another group receiving high dose dexamethasone. The company was repeatedly alerted about the unsuitability of the comparator choice for regulatory decision making.

Failure to follow its recommendations

The main study supporting the marketing authorisation of **S-1** (tegafur/gimeracil/oteracil) in combination with cisplatin for the treatment of advanced gastric cancer was designed to show its superiority over 5-fluorouracil in combination with cisplatin. When the trial did not meet its objective, the sponsor company changed the primary objective from superiority to non-inferiority. EMA's guidance from 1999 admitted that "there is ample room for bias" if the non-inferiority margin is chosen after the data have been inspected.

Tolerance for questionable analytical practices

Trastuzumab received marketing authorisation in 2011 for locally advanced breast cancer. The main study supporting approval measured overall survival as a secondary endpoint. Although the predefined analysis did not show a statistically significant survival benefit, EMA concluded that "the strongest evidence of benefit was provided by overall survival results" on the basis of an exploratory analysis that achieved significance after data were excluded from one of the participating centres. In the five year follow-up of the trial, investigators concluded the difference between groups in overall survival did not reach significance.

Panitumumab was approved in 2011 as a second line treatment for colorectal cancer on the basis of a randomised controlled trial with the coprimary endpoints progression-free survival and overall survival, analysed using a P value of 0.01 and 0.04, respectively. At the time of approval, primary analysis showed a borderline statistically significant benefit in progression-free survival, which the EMA did not consider robust. There was no statistically detectable overall survival benefit. However, a later publication reported that the final analysis of this trial showed significant improvement in progression-free survival. Yet the P value for this analysis was 0.023, which did not meet the investigators' prespecified threshold.

Courtney Davis, Department of Global Health and Social Medicine, King's College, London, and Huseyin Naci, LSE Health, London

For example, the EMA approved vinflunine as a second line treatment for metastatic transitional cell carcinoma of the urothelial tract in 2009 on the basis of a potentially biased analysis. But the UK National Institute for Health and Care Excellence (NICE) was less convinced, implying the evidence used for regulatory approval did not show the drug to be effective, and didn't recommend it.

Although the exact reasons for rejection aren't always clear, an assessment body analysis obtained by *The BMJ* shows that most European states have also taken a less favourable view of vinflunine than the EMA.

For patients, approval of such drugs may lead to unfulfilled hope, fuelled by patient organisations. In response to NICE's decision, Action on Bladder Cancer, a charity supporting patients and promoting research, wrote to the agency to complain that: "Patients with metastatic bladder cancer are disadvantaged by the lack of a second line treatment option. Study 302 is the first trial to show a survival benefit and we feel that vinflunine should be available for this relatively small group of patients."

Uncertainty is compounded by unproven drugs being used as comparators. Despite the questions around vinflunine, for example, it is now being used as a comparator in trials. On its website, the patient charity Fight Bladder Cancer has highlighted an ongoing study of a drug called PDL3280A for patients with advanced or metastatic bladder cancer. This, they say, compares chemotherapy with either paclitaxel or vinflunine. But regulatory sanctioning of a comparator that lacks robust evidence of efficacy, means the cycle of weak evidence and uncertainty continues.

No one wants to say no to a cancer drug

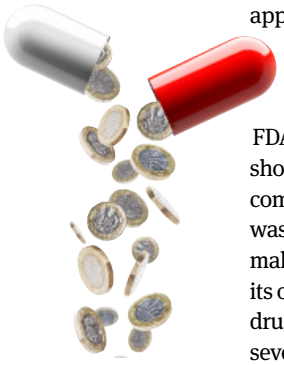
Vinflunine isn't an isolated example of questionable decision making. In 2011, the EMA licensed panitumumab in combination with other drugs as a second line treatment for colorectal cancer. This was despite the agency questioning whether the primary analysis showing a borderline statistically significant benefit in progression-free survival was robust. Indeed, the EMA rejected the drug but later reversed its opinion.

In the words of one EMA adviser who spoke to The BMJ, however, "no one wants to say no to a cancer drug." When NICE invited Amgen, panitumumab's manufacturer, to submit evidence for approval to use on the NHS, the company declined to do so. They intimated that there wasn't sufficient evidence to determine the cost effectiveness. Again NICE didn't recommend it.

Most European funding bodies have also turned down panitumumab for second line treatment for colorectal cancer. However, the published study does not reflect the questions over the statistical analyses, concluding that panitumumab "significantly improved" progression-free survival and there was "a trend toward" improved overall survival.

Health technology assessors are in an invidious position—if they refuse to reimburse and a drug later turns out to be an important therapeutic advance, then patients have lost out because of the delay. If they reimburse and the drugs later turn out to be ineffective, have no clinically meaningful effects, or not to be cost effective then patients may have been unnecessarily subjected to toxic drugs and scarce healthcare resources have been wasted.

17 drugs for **23** different indications were culled from the Cancer Drugs Fund in 2015



This hype coupled with underlying concerns about the quality of trials can cause confusion. In England, pomalidomide, an immunomodulatory drug for refractory multiple myeloma wasn't available, then was, then wasn't, then was again. The drug was approved by regulators in Europe and the US despite questions over trial design.

Correspondence between the FDA and Celgene, the trial sponsor, shows the US agency cautioning the company that its choice of comparator was unsuitable for regulatory decision making. The FDA ultimately ignored its own advice and approved the drug regardless. The EMA approved it several years later.

When NICE rejected the drug for use in the NHS because of the poor comparator, Celgene claimed that it was chosen only after consulting with the regulators. Pomalidomide subsequently went onto England's Cancer Drugs Fund, an extra source of funding, only for budgetary

PATIENT COMMENTARY: THE MODEL HAS FAILED

The cost of cancer drugs is skyrocketing: prices increased by 10% every year between 1995 and 2013. More and more we're seeing cancer drugs being priced off the NHS—as is the case with secondary breast cancer drug palbociclib, currently under review after it was rejected by NICE earlier this year because of cost.

Another really hard burden to bear for patients is that so many new drugs don't offer much of an improvement on existing ones: the independent drug bulletin Prescrire found that only 7% of 1345 therapeutic drugs assessed between 2000 and 2013 offered "a real advantage" when compared with drugs that were already available. More than half were "me too" products that aim to take a share of a competitor's market but offer little or no additional therapeutic value for patients.

As someone with secondary breast cancer, I find it incredibly upsetting that drugs which could be of benefit have such a high price tag that the NHS can't afford them. And at the same time, we are not seeing the development of the new medicines that we need; nor are we getting quick enough access to those that have already been developed.

It's clear to me and thousands of other patients that our research and development model has failed. Just Treatment, a patient led campaign with no ties to the pharmaceutical industry, is calling for a system that rewards and promotes innovation, so that more effective and accessible cancer medicines are brought within reach. An alternative model such as delinkage—whereby drug prices are decoupled from research and development costs—would reward companies for bringing new, effective drugs to market while ensuring these medicines remain an affordable public good. We need new drugs to be made available quickly, safely, and at affordably.

"We need a system that rewards and promotes innovation"
Emma Robertson

Emma Robertson, Just Treatment

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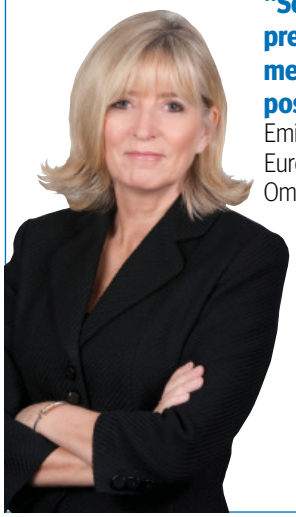
EUROPEAN REGULATOR UNDER SCRUTINY

Some aspects of the EMA's regulatory process are coming under scrutiny—not least the scientific advice offered companies seeking approval for their drugs.

According to Guido Rasi, EMA's executive director, early dialogue with medicine developers allows the agency to give scientific advice and help with protocols to "provide methodological direction and discourage the production of irrelevant or substandard data."



"Some presubmission meetings may pose some risks"
Emily O'Reilly, European Ombudsman

Currently, the scientific advice EMA gives is not publicly available, preventing its assessment. Some advocacy groups have reported that attempts to access such information have been thwarted by commercial confidentiality.

People both currently and formerly involved with EMA have told *The BMJ* that manufacturers see presubmission processes as a way to lobby the agency, repeatedly asking the same question until they get the answer they want, and this effect may impact on various aspects of trial design, conduct and analysis.

In July this year Emily O' Reilly, the European Ombudsman, launched a "strategic inquiry" into EMA's processes.

Although she recognised that "these activities help the development and availability of high-quality, effective and acceptably safe medicines," such "activities may pose some risks."

She noted that the EMA sees presubmission meetings as a way to "enable medicine developers to establish contact with the agency staff who will be involved with the application."

The case of cancer drugs also raises question about inconsistency between funding and licensing decisions in Europe. One suggestion has been for the EMA to work alongside the

"Scientific advice discourages the production of irrelevant data"
Guido Rasi, EMA's executive director

organisations carrying out health technology assessments, which countries use to help decide whether to pay for a treatment.

On paper, joining up the EMA with health technology assessment might seem a quicker way of getting drugs to patients. But concerns are being raised that EMA standards might actually erode those applied by some health technology bodies. More importantly, perhaps, is that decisions about pricing and reimbursement should also be related to the gross domestic product of countries, which differs greatly across the EU. Differential pricing would not be possible if assessment was linked with EMA approval.

Furthermore, members of some health technology bodies say they are currently a barrier against poor regulatory decisions and worry that EMA's "regulatory capture"—whereby 89% of the agency's budget comes from the drug industry fees—may come to thwart their independence.

constraints eventually leading to it being removed in 2015. It was one of 17 drugs for 23 different indications to be included in the cull.

The delisting prompted both companies and charities to call for all interested parties to work together to find a better solution for patients, putting pressure on NICE. Noticeably, however, this did not necessarily include better evidence generation and better oversight from the EMA.

"This has been a unilateral decision by NHS England. What is missing is a willingness for all stakeholders to take part in collaborative discussion and work together," Wim Souverijns, general manager at Celgene UK and Ireland, said. "There is a role for companies to put pressure on stakeholders, including NICE and NHS England, to point out the implications of these changes."

This pressure may have worked for patient access and cost purposes. In 2016—after the company offered a confidential discount—NICE approved the drug because it became cost effective.

Regulator fit for purpose?

The inability of EMA to uphold its approval policies has implications for patients and budgets, and the scientific advice the agency gives is coming under much scrutiny.

The example of bevacizumab (Avastin) is a cautionary tale about how well the EMA can monitor, evaluate, and learn about products even after they are on the market. Yet the agency wants to push ahead with a programme allowing quicker access to drugs with immature data.

In June 2011, the FDA revoked bevacizumab's indication for metastatic breast cancer because it "has not been shown to provide a benefit, in terms of delay in the growth of tumors, that would justify its serious and potentially life-threatening risks. Nor is there evidence that [it] will either help women with breast cancer live longer or improve their quality of life."

But the drug is still licensed in Europe for metastatic breast cancer; the EMA withdrew the licence for only some uses. It said this was because the data on use in combination with paclitaxel have "convincingly shown to prolong progression-free survival of breast cancer patients without a negative effect on the overall survival."

Again the EMA's decision caused challenges for funders. Bevacizumab was rejected by NICE and was one of the most requested drugs under the Cancer Drugs Fund.

It was another of the drugs delisted in 2015, leading to disappointment of patient groups. "People with incurable breast cancer can only watch from the sidelines as life-extending treatments are debated again and again and vital options disappear," said the charity Breast Cancer Care. But patients will continue to have their hopes dashed if regulators approve drugs using designs that are not methodologically rigorous.

Deborah Cohen, associate editor, *The BMJ*
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