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## A letter to the next secretary of state for health

*The BMJ* provides a checklist for a healthy NHS

ELECTION 2015

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Dear Secretary of State,

At the time of writing we don't know who this letter is addressed to or what coalition or partnership deals will be needed to form a government. What we do know is that the next five years are likely to be the most challenging and decisive that the NHS in England has ever faced. Our intention in writing this letter is to set down in a non-party political way what we believe is needed to heal the NHS.

Let us start with the current situation as we see it. Still reeling from the costly and distracting Lansley reorganisation, with virtually flat-line funding in real terms since 2010,[1] and the growing demands of an ageing population with increasingly complex needs, England's NHS is stretched close to breaking point. Extreme cuts to social care have exacerbated the pressures, causing knock-on effects across the service.[2] Waiting times for treatment are the longest for many years.[3] Staff morale in many parts of the service is at rock bottom because of real terms pay cuts and the relentless workload. Many GPs are retiring early, and new recruits are thin on the ground.[4] Patient safety is now at risk, with 13 NHS trusts currently in special measures because of concerns about the quality of care being delivered.[5] While services across the country continue to deliver outstanding care, the pressure is unsustainable.

The NHS's finances have now have been cut to the bone. Efficiency savings during the last parliament came, in reality, largely from pay restraint and cutting the prices paid to providers. All the main political parties have acknowledged that these are tactical "solutions" that will destabilise the NHS if they are continued.[6]

The cumulative deficit of hospital trusts and other NHS providers in England reached a record £1bn (€1.4bn; $1.5bn) last year [7] and is expected to double by the end of 2015-16. Eighty per cent of acute trusts are now in deficit.[8] Simply to maintain current levels of service, we are told that a funding gap of £30bn must be filled. In his *Five Year Forward View*,[9] NHS England's chief executive, Simon Stevens, demands savings of £22bn over the next five years. The plan


**Health is not a commodity; market competition has fragmented the NHS, with the evidence for its effectiveness patchy at best**

proposes new models of care, which alongside better self care and an expansion of prevention and public health, may help to fill the funding gap. But this level of saving will still require efficiency gains never before achieved by the NHS, and a further £8bn is needed from government by 2020 just to stand still. The additional election promises—seven day working, guaranteed shorter access times, and more GPs and nurses—have been described by Mark Porter, the BMA's chairman, as "outlandish and unachievable."

### Back to basics

What then does England need from you during your stewardship of its health service? Firstly, we ask that you give an unshakable commitment to providing a national health service, underpinned by core principles of universal health coverage, equity of access, and the provision of high quality care without fear of financial hardship. The NHS must remain publicly funded and free at the point of need. Secondly, we ask you to resist the temptation to undertake major top-down reorganisation. Instead those working in the NHS need breathing space and training and resources so they can create and evaluate new ways of delivering care in full partnership with patients.

Thirdly, we urge you to focus on collaboration not competition and marketisation. Too much faith has been placed in the internal market as the cure to all of the NHS's ills. Health is not a commodity; market competition has fragmented the NHS, with the evidence for its effectiveness patchy at best.[10-12] Concern about the speed of marketisation, and the prospect of the NHS being broken up for further privatisation, has led to calls for the repeal of the Health and Social Care Act.[13] Whether this would roll back the worst excesses of marketisation remains unclear.[14] Think carefully before embarking on any legislative change; be sure a repeal of the act has the effect of largely removing competition and market mechanisms from the NHS and isn't just a symbolic gesture.

Fourthly, we ask you to restore a strong voice and protected funding for public health. Pressure on the NHS is driven in large part by the wider social determinants of health. The past 30 years have seen a steady decline in the influence of public health as an independent voice and a national resource to drive and evaluate health improvement. Since the transfer of public health to local authorities, funds have been raided to address shortfalls elsewhere.[15] We urge you to ring fence public health budgets to protect vital services. A strong national public health voice is essential for health promotion, disease prevention, and social justice.

Fifthly, the NHS needs good transparent governance and less political interference. Unusually for a document of its type, the *Five Year Forward View* has been widely welcomed across the NHS. Give your backing to NHS England's chief executive and resist the temptation to micromanage. As Anita Charlesworth of the Health Foundation says,[14] your job is now to provide "hope and vision" rather than a shopping list of new policies.

Finally, we come back to the money. We urge you to properly fund England's health service. The UK spends the joint lowest of any G7 country on healthcare as a proportion of gross domestic product,[16] and the NHS is widely acknowledged to provide the most cost effective care of any developed nation.[17] The NHS is not unaffordable, but if it is deprived of the funds it needs to meet demand effectively, it could become so.[18] History will not forgive another health secretary whose actions contribute to its decline. Let this be the five years that secure the NHS's future as the best and fairest health service in the world.

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FEATURE, p 14; ESSAY, p 16; OBSERVATIONS, pp 25, 26

**thebmj.com**

- Research: The association between kidney function and major bleeding in older adults with atrial fibrillation starting warfarin treatment (*BMJ* 2015;350:h246)
- Clinical Review: Anticoagulation in atrial fibrillation (*BMJ* 2014;348:g2116)

**Given the variability in drug absorption that influences bleeding risk, patients taking newer oral anticoagulants might benefit from some kind of monitoring**

# Safety of new oral anticoagulants

## We need reliable tools to predict risk of gastrointestinal bleeding

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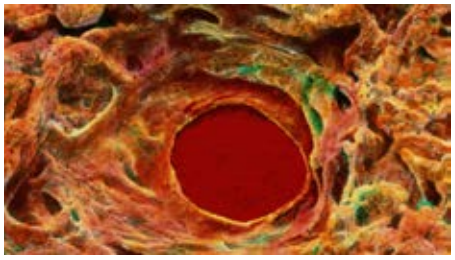
Two linked papers report additional evidence on the risks of gastrointestinal bleeding among patients taking the novel oral anticoagulants dabigatran and rivaroxaban.[1 2] From a database of more than 100 million US adults, Abraham and colleagues identified almost 220 000 new users of dabigatran, rivaroxaban, or warfarin between November 2010 and September 2013.[1] In their comparison of propensity score matched patients, the risk of gastrointestinal bleeding increased significantly with age for both new oral anticoagulants, relative to warfarin. By age 75, the risk of gastrointestinal bleeding associated with rivaroxaban exceeded that with warfarin, for patients with or without atrial fibrillation. Among patients taking dabigatran, the association between older age and higher risk was confined to those with atrial fibrillation, although the data included very few patients without atrial fibrillation taking this drug.

In a second study, Chang and colleagues found no significant differences in risk of gastrointestinal bleeding between the newer agents and warfarin in a propensity weighted analysis of 46 000 members of a commercial insurance plan who had new prescriptions for warfarin, dabigatran, or rivaroxaban.[2] Confidence intervals were wide, however, and the authors were unable to completely rule out the possibility of a greater risk associated with the new agents.

Post-marketing reports on the risk of gastrointestinal bleeding associated with the newer oral anticoagulants are conflicting, owing in part to differences in the doses used and the indications for specific drugs. Several studies suggest a higher risk of gastrointestinal bleeding associated with the newer agents among patients with atrial fibrillation. The RE-LY trial of dabigatran found that risk of gastrointestinal bleeding was 50% higher (compared with warfarin) among patients with atrial fibrillation who were given dabigatran 150 mg but no higher among those given 110 mg.[3] A meta-analysis reported a 52% higher risk of



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**Complexity in the real world**

gastrointestinal bleeding among patients with atrial fibrillation taking dabigatran compared with warfarin,[4] and studies of older Medicare beneficiaries with atrial fibrillation also found a higher risk associated with dabigatran.[5 6]

Similarly, the ROCKET-AF trial found a higher risk of gastrointestinal bleeding associated with rivaroxaban compared with warfarin.[7] A meta-analysis determined that the risk in patients taking rivaroxaban exceeded the risk with warfarin by 47%.[4]

Patients receiving oral anticoagulants for atrial fibrillation are typically older than those receiving anticoagulation for treatment or prevention of recurrent venous thromboembolism. Importantly, no clinically relevant increases in major bleeding events were noted in the RE-COVER, RE-MEDY, and EINSTEIN trials that established the efficacy of dabigatran and rivaroxaban for prevention of venous and pulmonary embolism.[8 9] Moreover, subsequent meta-analysis of these trials found a significant reduction in gastrointestinal bleeding for new oral anticoagulants compared with warfarin.[10] However, the patients in these trials were relatively young, with a mean age below 60.

In contrast, the mean age of participants in RE-LY was 71 years and the median age in ROCKET-AF was 73 years. Data from both trials suggest that rates of drug clearance decrease with age.[11] Although this is also true for warfarin, the increased bioavailability of the newer agents that occurs with age seems to induce a greater increase in bleeding risk than does the same change in bioavailability of warfarin. This is consistent with the findings of Abraham and colleagues.[1] The increased bleeding risk associated with dabigatran in RE-LY was also largely attributed to patients over the age of 75.[12]

Given the variability in drug absorption that influences bleeding risk, patients taking newer oral anticoagulants might benefit from some kind of monitoring—perhaps not as frequent as for patients taking warfarin, but at least once or twice to guide decisions about dose. Unfortunately, no consensus exists about which tests to use, as "standard" tests for coagulation are not adequate in patients taking the newer agents, and results vary depending on laboratory procedures.[13] Studies have suggested that checking plasma drug concentrations may be the best way to guide therapy,[11] but such tests are not yet commercially available.

### Dose: another variable to add to the mix

Studies based in the United States by Abraham, Chang, and others evaluate dabigatran only at doses of 150 mg and 75 mg, most commonly 150 mg; dabigatran 110 mg is not approved there. Importantly, European guidelines recommend dabigatran at the 110 mg dose for older patients and those at high risk of bleeding.[14] In one study using the Danish National Registry,[15] more than 95% of patients over 80 who were taking dabigatran, received the 110 mg dose. Larsen et al, using the same data source, reported a 40% lower risk of gastrointestinal bleeding in patients taking dabigatran 110 mg, compared with warfarin.[16 17] The recommended dose of rivaroxaban depends on the indication for treatment and the presence or absence of renal impairment. One meta-analysis of clinical trial data suggests that only the highest dose (20 mg) is associated with an increased risk of gastrointestinal bleeding.[17]

The studies by Abraham and Chang add to a complex picture of real world risk associated with the newer drugs relative to warfarin.[1 2] Although older age is predictably associated with increased risk of gastrointestinal bleeding during treatment with any anticoagulant, how age influences the relative risk among different agents is not entirely clear. We need better ways to predict which patients are at highest risk of gastrointestinal bleeding, especially during treatment with newer oral anticoagulants. Monitoring of drug concentrations in patients taking newer agents, combined with a range of possible dose options, may hold the key to optimising the safety and effectiveness of these unfamiliar drugs.

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RESEARCH, pp 11, 12

**thebmj.com**

- Research News: Physical therapy is as effective as surgery for lumbar spinal stenosis (*BMJ* 2015;350:h1827)
- Practice: Avoid surgery as first line treatment for non-specific low back pain (*BMJ* 2014;349:g4214)

**Is our hunger for new techniques based on little more than a gut feeling that new and smaller is always better and, if so, is it ethically justifiable to "test" these new techniques on patients?**

# Minimally invasive surgery for lumbar spinal stenosis

## As good as open laminectomy, but no better

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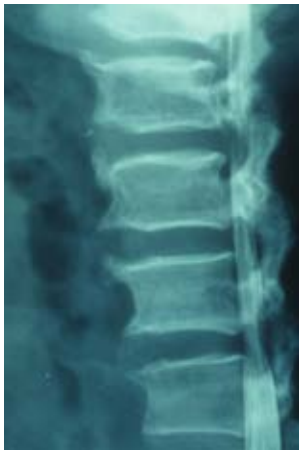
Recent trends in spine surgery, such as endoscopic and other "micro" techniques, promised less invasive procedures and better outcomes compared with conventional open techniques for decompressing nerves. Minimally invasive techniques are popular with patients, promoted by industry, and increasingly used by surgeons.[1] However, recent studies have failed to report any clear benefits for patients.[2] Is our hunger for new techniques based on little more than a gut feeling that new and smaller is always better and, if so, is it ethically justifiable to "test" these new techniques on patients? In a linked paper Nerland and colleagues provide some hard evidence to help inform these important debates.[3]

Their study compares the "old" standard surgical treatment for spinal stenosis (open laminectomy) with a newer and less invasive alternative (microdecompression). Microdecompression is a procedure to decompress the lumbar nerves by removing a minimal amount of bone and the ligamentum flavum but leaving the spinous process and the supraspinous and interspinous ligaments intact. The authors analyse data from a large, well organised and comprehensive national registry in Norway (the Norwegian Registry for Spine Surgery, NORspine). Thirty six out of 40 centres performing lumbar spine surgery in Norway record data prospectively in NORspine, making it a unique national resource for spine research.[4]

Nerland and colleagues identified 885 eligible patients (out of 2745 screened), and 81% completed the one year follow-up. Microdecompression and laminectomy were associated with similar improvements in disability scores and quality of life over one year, and the two techniques were statistically equivalent. In predefined subgroup analyses, microdecompression and laminectomy were also equivalent in older people and those with obesity. However, patients treated with laminectomy had more complications than those treated with microdecompression, and the difference was significant in one of the two main analyses (15.0% *v* 9.8%, P=0.018). Patients treated with microdecompression had significantly shorter hospital stays (1.9 *v* 3.4 days). The authors concluded that patients with stenosis of the lumbar spine should be treated with microdecompression to prevent instability and because treatment with microdecompression leads to shorter hospital stays and fewer complications.

The authors mention that microdecompression may also induce less postoperative instability. They did not, however, report any reduction in instability associated with microdecompression, and there is no solid evidence that more invasive surgery causes greater instability or that less invasive surgery causes a better clinical recovery.[5]

As the authors claim, large clinical registries allow the effectiveness and safety of widely used procedures to be monitored and evaluated. Cautious interpretation of observational data from registries is, however, always advisable. Clinical outcomes in this study were equivalent in both treatment groups despite the small differences in complication rates and lengths of hospital stay and despite the large patient sample. Interpreting small differences in outcomes can be difficult when data are obtained from big registries. The risk of confounding by patient selection is high in non-randomised studies: small differences in results can be due to variations in case mix between the groups, along with differences in management or different postoperative regimens. Laminectomy is considered a more old fashioned treatment, but it could still be used in centres where fast track surgery is not available. It is even questionable whether patients with large bony decompressions really do need a longer hospital stay than those requiring less invasive surgery. When a provider switches to microdecompression as the preferred option, the mindset also shifts into the "less is better" paradigm: patients will be admitted on the day of surgery instead of the day before, and discharged the next day instead of two days later.



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**Is less more, less, or the same?**

Surprisingly, the authors chose an "equivalence" design and powered their study accordingly, judging that the two options would be equivalent if the outcome difference between them after one year was eight points or less on the Oswestry disability index. A superiority design is more usual and arguably more useful for evaluations of alternatives to traditional laminectomy,[6] and a clearer justification for the authors' choice would have been helpful.

Ideally, registry based research should be confined to comparisons of treatments that are both known to be safe, because many patients have been treated by the time results are available from this kind of study. As Nerland and colleagues mention, minimally invasive surgery for spinal stenosis was accepted and used widely with minimal supporting evidence, and before safety was fully established. Nevertheless, big data studies such as theirs are useful because patients in registries are more typical of real world practice than the over-selected patients usually included in randomised controlled trials. Registry based research will be an important contributor to long term evaluations of surgical treatments and has already proved useful—for example, in evaluating the long term side effects of drugs.

### Can do better

Nerland and colleagues' study nicely demonstrates the potential benefits of registering patient outcomes associated with daily clinical practice. Studies of big data are clearly useful for evaluating surgical treatments and add a different dimension to the results of more selective randomised trials. In this case, however, we still have no evidence that minimally invasive surgery works any better in the long term for patients than more traditional open decompression techniques. In concordance with the IDEAL framework phase 3, all new surgical techniques must be evaluated more robustly in the future, starting with high quality randomised trials and cost effectiveness analysis,[8] followed by good long term follow-up using registries such as NORspine.[9]

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RESEARCH, p 13

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- Views & Reviews: We need a drug formulary for obese people (*BMJ* 2015;350:h1356)
- Research: Comparison of metformin and insulin versus insulin alone for type 2 diabetes (*BMJ* 2012;344:e1771)

**A Cochrane review concluded that there is no evidence from prospective or observational studies that metformin is associated with lactic acidosis**

# Using metformin in the presence of renal disease

## Current guidelines are too restrictive, and many patients who could benefit are missing out

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In January, the electronic Medicines Compendium (eMC) updated the Summary of Product Characteristics for Glucophage (metformin), approved by the UK Medicines and Healthcare Products Regulatory Agency (MHRA). The summary states that "Metformin may be used in patients with moderate renal impairment, stage 3a (creatinine clearance [CrCl] 45-59 mL/min or estimated glomerular filtration rate [eGFR] 45-59 mL/min/1.73 $m^2$) only in the absence of other conditions that may increase the risk of lactic acidosis . . . If CrCl or eGFR fall <45 mL/min or <45 mL/min/1.73 $m^2$ respectively, metformin must be discontinued immediately."[1] This is reiterated in the patient information leaflet.

Interestingly, the summary for generic metformin states that "Renal failure or renal dysfunction (creatinine clearance <60 ml/min)" is a contraindication to use. In the face of burgeoning levels of type 2 diabetes and associated renal disease, we believe that this restriction is too conservative and will deny an important drug to many thousands of people with diabetes who are likely to benefit from its important clinical effects and have few alternative treatments.

Metformin is recommended as the first line oral hypoglycaemic drug for patients with type 2 diabetes in national and international guidelines.[2 3] The drug is the only one of many diabetes drugs to show cardiovascular benefits, especially in overweight or obese patients with type 2 diabetes.[4] Metformin is also useful in overweight patients with type 1 diabetes,[5] women with gestational diabetes or polycystic ovary syndrome,[6] and in people at high risk of developing diabetes.[7] There is some epidemiological evidence that metformin may reduce the risk of cancer in people with type 2 diabetes.[8] The drug has been safely and widely prescribed for over 50 years and benefited millions of people. The adverse gastrointestinal effects of metformin are usually mild and temporary, and the drug does not induce weight gain. Use of metformin with insulin is both insulin dose sparing and weight sparing.

### Risk of lactic acidosis overstated

Around a quarter of all patients with type 2 diabetes develop diabetic nephropathy, and the condition is the commonest cause of end stage renal failure in most developed countries. The concerns over metformin and renal impairment arise from the perceived risk of lactic acidosis in such patients. Although metformin overdose may be linked with lactic acidosis, a recent systematic review of cases reporting a link between metformin and lactic acidosis suggests no direct causal link and that other factors (such as sepsis or hepatic or cardiac failure) may be implicated.[9] Indeed, a Cochrane review on the subject concluded that there is no evidence from prospective or observational studies that metformin is associated with lactic acidosis, nor even associated with raised lactate concentrations.[10] This is supported by a review of the General Practice Research Database, which showed a crude rate of lactic acidosis of 3.3 per 100 000 patient years among people taking metformin, compared with 4.8 per 100 000 patient years among those taking sulfonylurea.[11]

Nevertheless, the relatively unfounded concerns mean that large numbers of patients with type 2 diabetes are not receiving metformin, and indeed this number could grow if pharmaceutical guidelines are adhered to. A recent survey in the US suggests that if all patients with diabetes and eGFR >30 mL/min/1.73 $m^2$ were prescribed metformin, roughly one million more people would be taking the drug.[12]

### Wider use

Premature cessation of metformin in patients with renal disease may expose them to considerable harm. In clinical practice, we often see premature cessation of metformin leading to poor glucose control, and further deterioration in renal function. Diabetic patients with renal disease have a higher cardiovascular risk, and denying them metformin may increase this risk. Although several new drugs are available for use in people with type 2 diabetes, most are contraindicated or not licensed for use in renal impairment. Glitazones are associated with weight gain, fluid retention, heart failure, and possibly postmenopausal fractures. Saxagliptin is associated with heart failure, and sulfonylureas and insulin are associated with hypoglycaemia and weight gain—adverse effects that are particularly concerning in patients with renal disease.

Guidelines from the UK National Institute for Health and Clinical Excellence (NICE) suggest that metformin dose should be reviewed at an eGFR of 45 and stopped at an eGFR of 30.[2] There is accumulating evidence, however, to suggest an important pharmacogenetic component to metformin metabolism, and this may enable some patients to continue the drug at lower levels of renal function.[13] Dosing may be guided by wider use of plasma metformin concentrations in such patients, although further research evidence is required before this practice can be advocated.

Nevertheless, NICE guidelines are pragmatic and can safely be used in clinical practice. We would encourage clinicians to use these guidelines and reassure patients that metformin is perfectly safe in stable renal disease. Patients should, however, be advised to stop metformin during periods of acute illness (such as gastrointestinal upset or other infections), where renal function may acutely deteriorate, and restart metformin when they have recovered.

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