comment

> As outsourcing has become normal the debate on what "privatisation" of the NHS amounts to, or what it would look like, is magnified

NO HOLDS BARRED Margaret McCartney

Should the NHS rely on outsourcing?

Carillion, the outsourcing company that provided the NHS with cleaners, porters, and catering, has hit the buffers. The only people surprised by this are those who haven't been paying attention.

Outsourcing as a principle has been beloved of governments of red and blue hues over the past couple of decades.

As outsourcing has become normal the debate on what "privatisation" of the NHS amounts to, or what it would look like, is magnified. What does it matter who provides a service, as long as it's under the banner of the NHS and adheres to the contract? We don't expect (or want) the NHS to make paper, build ambulances, or manufacture CT scanners: private involvement in the NHS has always happened, and outsourcing is not new. This logic has underpinned the recent history of NHS contracting.

The annual value of outsourcing work now offered under tender from the NHS is £5.9bn. Circle was awarded a contract to run Hinchingbrooke Health Care NHS Trust in 2010, only to hand back its contract to the NHS in 2015 with requests for government bailouts.

In 2015 Capita took on a £1bn, seven year contract for "back office" functions in England. Repeated disruptions followed, such as GP trainees' salaries going missing, syringes not being supplied, GPs being unable to get onto the performers list, and notes going missing. In the wake of these, the National Audit Office has announced an investigation into the Capita deal.

And recall that Atos—which prematurely ended its contract supplying medicals to the Department for Work and Pensions because of "quality concerns"—subcontracted work to other companies, as well as back to the NHS.

Ah, some might counter: but GPs are also private businesses. That may be so, but I don't compete with other practices in my area in the way outsourced service providers compete with one another. But the GPs' NHS contract does allow for competition between practices, and some new kinds of general practice—especially those operating online—increasingly exploit this to compete for patients who are likely to use fewer resources.

It's all about efficiencies, say the management consultants who have recommended the wider use of outsourcing. So, if harmless efficiency is possible, why can't the NHS do it and keep the savings for itself? And if better efficiency isn't possible, and striving for it leads to active harms, surely it's better for us to ensure that avoidable damage isn't done. Devolving responsibility to companies that are immune to freedom of information requests, and frequently bailed out by the taxpayer, is not the way to do it.

Margaret McCartney, general practitioner, Glasgow
margaret@margaretmccartney.com
Twitter: @mgtmccartney

Cite this as: *BMJ* 2018;360:k670

PERSONAL VIEW Giles Maskell

Are we ready for the "new chest x ray"?

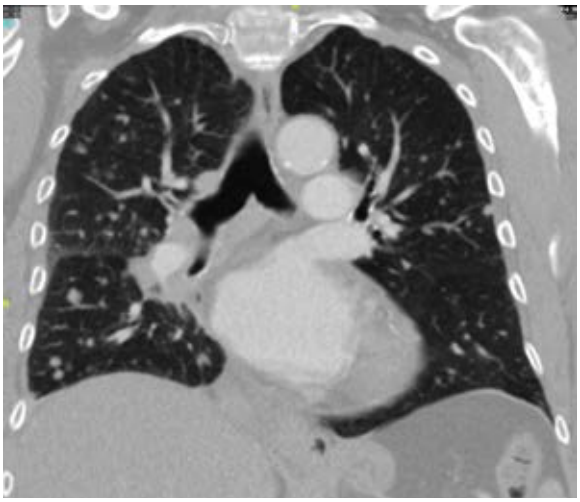
What would we need if we seriously contemplated replacing chest radiography with CT scanning in acute care?

The medical registrar was on the phone for the third time that morning. "Another CTPA?" I asked, aiming for a tone of polite surprise. She said, "Haven't you heard? It's the new chest x ray."

Computed tomography pulmonary angiography (CTPA) was introduced into clinical practice about 20 years ago. It has obvious appeal as an accurate test for pulmonary embolism, a common condition that can present acutely, is known to be hard to diagnose, and is sometimes fatal. And, unlike the traditional alternative—the perfusion lung scan—CTPA can suggest or exclude a range of other possible diagnoses. It has proved very popular, to the point where concerns have been raised that its use may have resulted in potentially harmful overdiagnosis.

Chest radiography has been around for a long time, and familiarity can perhaps blind us to its deficiencies, of which the inability to diagnose pulmonary embolism is only one. For example, about a quarter of lung cancers and half of all rib fractures are not detected by radiography. It makes no contribution to diagnosing asthma, coronary heart disease, or a range of other cardiorespiratory conditions until severe complications have developed. It provides very little functional information and, to put it bluntly, many people die after normal findings from chest radiography. And yet it retains a central role in the assessment of patients with acute medical problems, being almost a rite of passage in the admission process.

In recent decades the use of plain radiographs in many other clinical circumstances has come under scrutiny. The limitations of the abdominal x ray in patients with acute abdominal pain are widely accepted, as the greater use of ultrasound, and particularly CT scanning, has made its deficiencies glaringly apparent. X rays of the spine for trauma or back pain are now indicated only in specific circumstances, replaced when necessary by CT or magnetic resonance imaging in patients when imaging is essential to managing their treatment. For how much longer will



SPL

CT scans of A&E patients' chests have made the deficiencies of x ray glaringly apparent, but outcome evidence is in short supply

We would need a new generation of low cost, accessible, low dose CT scanners in every emergency room

ACUTE PERSPECTIVE David Oliver

Getting serious about preventing ill health

It's hard to attend any conference or read any report on health service reform without prevention of ill health featuring prominently. What might once have seemed a radical proposition is now an orthodoxy—but people commenting still advocate a greater focus on prevention and early intervention as if it's a revelation, even for those in government.

The arguments advanced for prevention contain two broad elements. First, our health services are still too centred on responding to ill health, especially acute illness in excessively hospital based models. We therefore need a shift of resources and approaches to ensure that more people remain well for longer (primary prevention) or are supported to self manage any long term condition to reduce complications, slow progression, and maximise wellbeing (secondary prevention).

Politicians are far more likely to be judged on how health services perform right now, for the sickest people

Second, a shift towards prevention requires interventions throughout the whole life and a focus on reducing health inequalities, as the antecedents of ill health are cumulative and synergistic. Conventional medical care is only a small part of the picture, and many of the determinants of physical and mental health lie in wider communities, universal public services, and private and voluntary sectors. Allied to this should be a focus on maximising the health assets of citizens rather than on disease and health deficits.

Such arguments have been made in numerous high profile reports, including those by Derek Wanless for the Treasury, the House of Lords committee on NHS sustainability, and the University of Birmingham policy commission. Government policy documents, going back over several parliaments, are full of them.

In the face of these entirely sensible recommendations, the recent policy response in England has been to move public health from the NHS to local government, notionally to tackle the wider determinants of health and join up public health with other services. But local government budgets have been slashed since 2010: public health funding fell by around £200m under the 2010-15 coalition government. A

we continue to put the chest x ray at the heart of acute medical diagnosis?

A new future?

It may be worth thinking about what would be required if we were seriously to contemplate replacing the chest x ray with CT scanning in the acute setting. To start with, we would need a new generation of low cost, accessible, low dose CT scanners to be installed in every emergency room to produce the necessary scanning capacity. Traditionally, a brake on the use of CT scanning has been the appropriate concern over the implications of the higher radiation dose involved. But technological developments in dose reduction, to the point where CT images can be acquired with doses approaching those of a chest x ray, are challenging the relevance of this.

We would need to train staff to use these machines and many more to interpret the images. Existing programmes for teaching chest x ray interpretation to a wide range of healthcare practitioners would need to be augmented with CT teaching.

Less obviously, we would need increased understanding and tolerance of the inevitable incidental findings that would proliferate—an appreciation, for example, that a high proportion of adults admitted with acute medical conditions will have at least one small pulmonary nodule and that enlarged mediastinal lymph nodes are found in most acute conditions but only rarely indicate malignancy. A test that inevitably generates serial follow-up imaging would be of limited value.

Evidence of outcomes

Perhaps most importantly, we would have to establish an evidence base to show that CT does outperform the chest x ray in improving outcomes for unselected acute patients without causing additional harm. How well, for example, does CT scanning perform in answering the question posed by acute physicians everywhere: is this patient's breathlessness caused by infection, pulmonary oedema, both, or neither? Evidence is currently in short supply.

Is it conceivable that we could kick the chest x ray habit and employ more sophisticated imaging for those patients whose management really depends on the outcome? I don't know—but I suspect that the new chest x ray may still be a little way off.

Giles Maskell is a radiologist, Truro
gilesmaskell@nhs.net
Cite this as: *BMJ* 2018;360:k769

recent King's Fund analysis showed a further 5% cut in public health funding since then and predicted another £88m of public health cuts for 2018 that will affect sexual health, smoking cessation, and drug and alcohol interventions.

These cuts also affect transport, leisure, social services, and funding for the voluntary organisations, day centres, and libraries that help people retain independence and stay connected to the community. Meanwhile, welfare changes, far from helping the "just about managing," have done little to help wellbeing or lessen inequalities for people living with poor health or disability. We've failed to implement a simple policy on minimum unit alcohol pricing despite clear evidence of benefit. And the government's recent childhood obesity strategy was neutered.

It can be difficult to "sell" major investment in prevention and public health—especially when primary and secondary care services are severely underfunded and where any "return on investment" dividend may not be seen for years. Politicians in office are far more likely to be judged on how health services perform right now, for the sickest people.

From now on, every time I hear people using policy rhetoric to make the case for prevention, I'll ask them, "So, what policies and funding do we have in place to back the paper talk and make it happen?"

David Oliver is a consultant in geriatrics and acute general medicine, Berkshire
davidoliver372@googlemail.com
Twitter: @mancunianmedic
Cite this as: *BMJ* 2018;360:k583

BMJ OPINION Kate Lovett

Muted cheer for the progress of women in medicine

This month we marked the 100th anniversary of some women gaining the right to vote in this country. I have to admit to feeling lukewarm about celebrating a partial victory.

Like many women, I come from a long line of suppressed ambition. Brought up in the 1970s, I was acutely conscious of a generation of women around me who had given up work to support their husband's careers.

I have come across many subtle and not so subtle barriers and power imbalances in my career, which have often been ignored and buried in the "notice and move on" part of my mind. When I was training, appalling sexism existed among too many clinical teachers. Even in 2016, when I was elected dean at the Royal College of Psychiatrists, the most common question asked of me at the time was, "And how is your husband coping?"

I like to think that things have got a lot better over the past 25 years. Training on unconscious bias is now routine, and appointment panels happen within working hours and with transparent processes. But there is still much to do. Gender is just one small aspect of diversity, and in terms of equality we know that, in many organisations and working cultures, this is far from a reality.

We know that, in many organisations, equality is still far from a reality

Our mothers and grandmothers fought hard to pave the way for future generations of women to succeed. And yet, all too often, our rigid systems and the lack of understanding about how to achieve full equality lets them down badly.

I'm relieved, however, that we are finally having this conversation, and I'm excited by the gathering momentum, seen at the recent Women's March, which I hope will mean that, in 10 years' time, we truly can celebrate how far we have come.

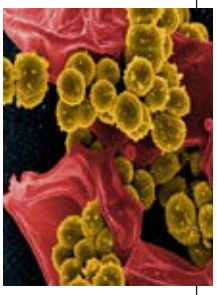
Kate Lovett is a consultant psychiatrist and dean of the Royal College of Psychiatrists

ANALYSIS

Research on multidrug resistance risks harming patients

Current approaches to testing new treatments for multidrug resistant bacterial diseases raise scientific and ethical issues for current and future patients, say **John Powers and colleagues**

KEY MESSAGES



- New antibiotics for life threatening infections are approved on non-inferiority hypotheses, which allow for lesser effectiveness
- It cannot be assumed that non-inferior effectiveness today will translate to future superior effectiveness
- When effective treatment exists, patients should not be exposed to increased risk of irreparable harm merely because they are easier to enrol in trials
- Superiority trials are feasible and more ethical in patients with resistant infections who have no treatment options
- Compared with non-inferiority trials they require smaller patient numbers, have no restrictions on previous treatment, and can include patient relevant endpoints

The threat of antibiotic resistance has fuelled legislative and regulatory efforts to develop new treatments for serious infections. Unlike in other therapeutic areas, most new antibiotics are approved without evidence of superior efficacy in clinical trials. Rather, regulatory authorities permit "non-inferiority" hypotheses. These may allow approval of antibiotics of lesser effectiveness than already approved drugs as a trade-off for other benefits such as fewer adverse effects.[1-5] Indeed, people claim that superiority hypotheses are unethical for antibiotic studies since they might expose patients in the control group to harm.[6]

A review evaluating US Food and Drug Administration approvals from 2009 to 2015 showed eight new antibiotics indicated for "serious and life threatening" diseases, with seven approved solely on evidence of non-inferiority. Recent FDA guidance supports extrapolating non-inferiority results to presume superior outcomes in patients without effective options.[2 5] But are drugs that are "non-inferior" today going to be superior tomorrow? Do non-inferiority trial designs expose today's patients with treatable life threatening infections to increased risk of harm by allowing antibiotics with less effectiveness onto the market?

Multidrug resistance and new antibiotics

Although resistant infections have been commonplace since the advent of antibiotics in the 1940s, effective treatment still remains for most patients. Resistance should be of most concern when the drugs affect morbidity and mortality. However, discussions about the rise of antibiotic resistance often focus on biomarkers of in vitro biological activity (eg, the minimum inhibitory concentration), assuming that these reflect patient outcomes.

Multidrug resistance is often described as decreased in vitro biological activity to multiple classes of drugs but does not consider other effective therapies. In fact, most patients do not have unmet medical needs since at least one effective therapy remains for them. When no effective treatment exists the unmet need is for a drug that is more effective (not equally or less effective) at reducing morbidity or mortality than current standards of care.[5]

Because smaller numbers of patients have no effective treatment option, premarketing trials of antibiotics usually recruit people with infections that remain susceptible to currently approved antibiotics.[2-7] For trials in patients with serious infections, ethical standards require use of already approved antibiotics as control drugs since randomisation to placebo would expose patients to increased risk of illness or death. These trials can therefore assess either superior effectiveness or non-inferiority to existing standard of care.

Superiority *v* non-inferiority hypotheses

Both overall and attributable mortality are substantial for many serious infections that are susceptible to antibiotics, such as ventilator associated pneumonia.[8] Nevertheless, it is suggested that newly developed antibiotics are unlikely to be superior to properly dosed comparators if the pathogen is susceptible to both agents.[9] Thus, superiority trials in patients with effective options are deemed "not feasible." Instead policy makers are pressured to accept evidence of lower quality for regulatory approval of new antibiotics.[10]

Regulators in the US and EU have seemingly settled on non-inferiority trials as the main approach to developing evidence for approval, on the primary basis that feasibility concerns are paramount. This raises four serious scientific and ethical questions.

1. Does the trial ask the right questions?

The rationale for using non-inferiority hypotheses is well known: "New interventions may have little or no superiority to existing therapies, but, as long as they are not materially worse, may be of interest because they are less toxic, less invasive, less costly, require fewer doses, improve quality of life, or have some other value to patients."[1 11]

But this rationale is rarely applied to antibiotic trials. Instead the rationale is that the antibiotics will have superior effectiveness in other populations, in other words, patients for whom the control drug is ineffective and who are excluded from non-inferiority trials. Non-inferiority trials are not usually focused on the resistant organisms for which new therapeutic options are most needed.[6] For antibiotic approvals from 1991 to 2011, only one of the 72 trial protocols or statistical analysis plans provided an explicit rationale for the acceptability of trade-offs between lesser efficacy and non-efficacy benefits.[12] None of

the trials delineated hypotheses or reported evaluation of non-efficacy benefits.

Rather than examining these trade-offs, investigators refer to trials as facilitating new antibiotics to market and providing incentives for drug companies.[6 7] As one commentator stated, "the less demanding but admittedly indirect hurdle of noninferiority . . . offers the potential to relatively rapidly identify drugs comparable in efficacy, jumpstarting antibiotic development."[13] But non-inferiority trials cannot show two interventions are exactly equal, and the results often do not rule out some level of harm because trials are often too small.[1]

2. Are non-inferior drugs today going to be superior tomorrow?

The idea that drugs that are non-inferior in today's patients will provide superior efficacy in future patients remains conjecture because the intended patient population has not been studied. Furthermore, there are compelling reasons to think the prediction is unlikely to come true.

Assumed future benefits are based on biomarkers of in vitro biological activity, termed an "improved microbiological spectrum of activity."[6] However, in vitro activity may not reflect direct patient benefits. Recent drugs with favourable in vitro activities compared with older drugs show increased mortality or decreased effectiveness in trials.

Patient factors are important. Those infected with resistant organisms are generally older, more critically ill, and have a greater incidence of renal insufficiency than patients with susceptible infections.[26] These factors influence the effects of drugs on patient outcomes independent of in vitro factors.[27-29] Antibiotics in patients with susceptible infections are less effective in patients with renal insufficiency, a group at greater risk of infection with resistant organisms.[5] Drugs that may be slightly less effective in non-inferiority trials may be substantially less effective in more critically ill, unstudied patients.[30] Heterogeneity of drug effects based on patient factors is common even in the absence of resistance.[31]

Finally, extrapolation to patients in whom the control intervention is not effective contradicts the basic premise of non-inferiority hypotheses. The interpretation of non-inferiority results applies only to patients in whom the control intervention is effective—a principle called the constancy assumption.[1 32]

Less effective drugs can still promote resistance to other effective drugs, worsening the problem of resistance they were intended to address. Use of newly approved antibiotics may also result in resistance, making them less effective in the future. But it is unlikely that manufacturers will delay use of new drugs since companies have limited periods of market exclusivity and business principles favour maximising current over future earnings.[34]

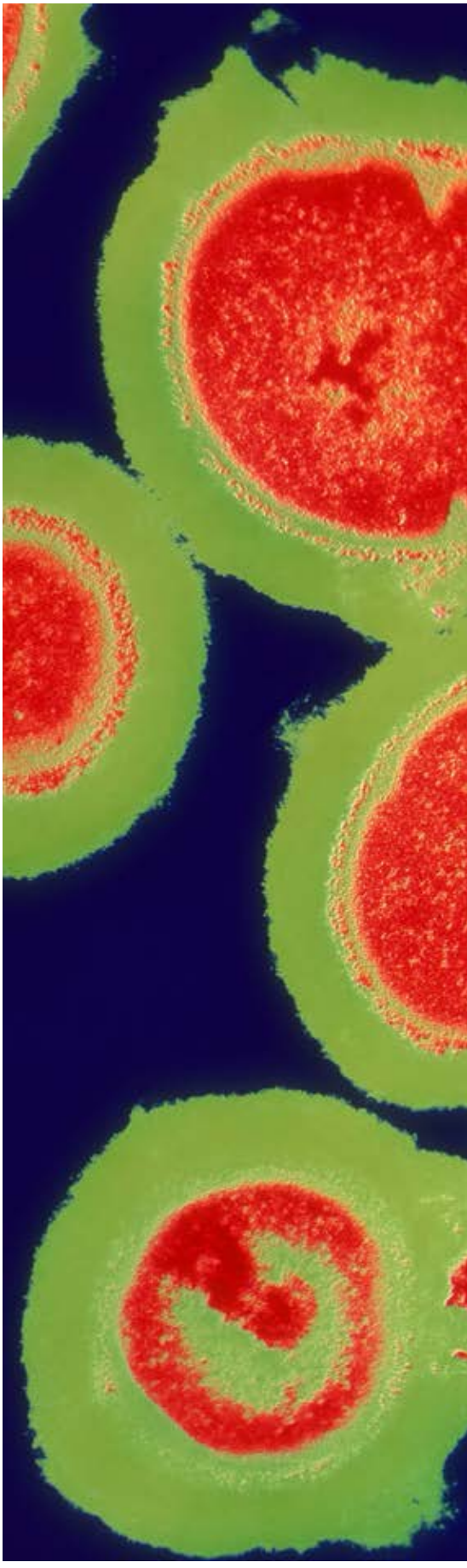
3. When is it ethical to expose clinical trial participants to potential increased harm?

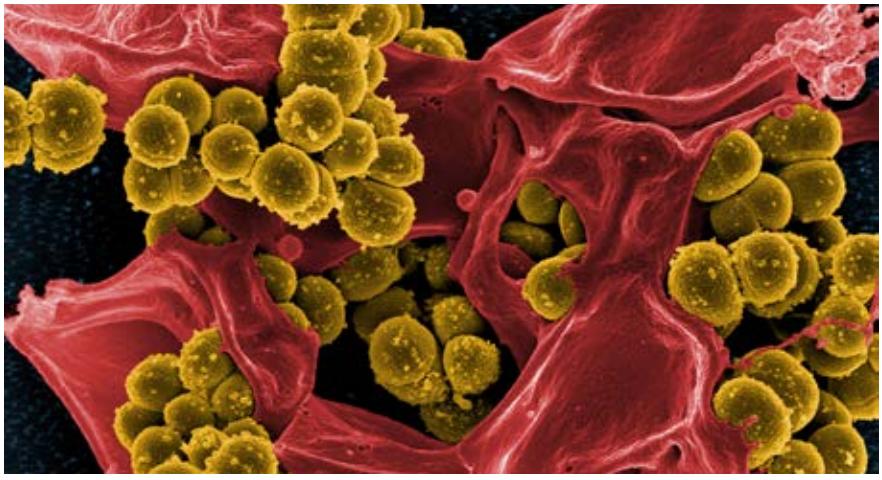
Non-inferiority trials include patients with currently effective options as surrogates for future patients with no effective options. But the benefit-risk assessments in these two populations should differ substantially, since patients with no options may be willing to accept more risk of harm than patients who have effective options. This raises ethical questions regarding beneficence and justice in the selection of research participants for non-inferiority trials and has implications for informed consent.[12 35]

The Declaration of Helsinki—the basis for modern ethical principles related to human subjects' experimentation—calls for caution not just in placebo controlled trials but also when exposing patients to interventions less effective than current standards of care. It states, "Patients who receive any intervention less effective than the best proven one, placebo, or no intervention will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention."[36]

Non-inferiority hypotheses are ethical in some situations (box). However, they are not ethical for trials of treatments for acute, life threatening infections that have effective therapies. Such patients may not find it acceptable to trade reduced effectiveness for fewer adverse effects or improved convenience. This is particularly true if lesser effectiveness translates to increased deaths or serious morbidity. Allowing rescue therapy for participants who do not respond to study interventions is a theoretical possibility, but it may not be achievable because of rapid disease progression in acute life threatening infections. Any delay in giving effective antibiotics may increase mortality.[41 42]

Patient input helps define the boundaries of acceptable trade-offs for non-inferiority hypotheses, but this input hasn't happened


SPL



Appropriate use of non-inferiority hypotheses

Non-inferiority hypotheses are best used when four conditions are met[37 38]:

- Older reliably effective therapy exists and these effects can be quantified
- The effect of older therapy on morbidity or mortality is so important to patients that they cannot be ethically randomised to placebo
- There are hypothesised benefits of new interventions other than improved effectiveness
- Potential decrements in effectiveness are based on patient input and are ethically acceptable when they do not place patients at risk for increased irreparable harm.[36]

over the past two decades.[12] International guidance cautions against allowing lower effectiveness in non-inferiority trials simply to reduce the required number of enrolled participants.[32]

4. What has been the performance of antibiotics approved after non-inferiority trials?

Although the current antibiotics of last resort were approved after non-inferiority trials,[7] the full track record of three decades of antibiotic approvals, primarily on the basis of non-inferiority trials, is less favourable. Of 61 antibiotics approved between 1980 and 2009, 26 (43%) were withdrawn by 2013, many for poor sales or safety and effectiveness problems.[43]

We might respond to the inadequate reimbursement for antibiotics by allowing regulatory agencies to approve new antibiotics with less evidence at earlier stages of development.[44] The US 21st Century Cures Act,[45] signed in December 2016, gave the FDA the green light to label new drugs for patients with "limited or no options."[15 46] But drugs with promising preclinical and early clinical data can fail to show benefits for patients in later stage trials.[47]

Moving forward: superiority trials and innovative trial designs

Only superiority hypotheses can determine whether new antibiotics meet the medical need of patients with multidrug resistant infections who currently have no treatment options. Superiority trials need not be large, nor impossible to recruit.[7 9] The Centers for Disease Control and Prevention estimates that two million people annually are infected with resistant pathogens in the US, leading to around 23 000 deaths.[50] It notes "many more die from other conditions that were complicated by an antibiotic resistant infection." These numbers should be a sufficient source of patients to study.

If these populations are difficult to find and enrol, then we should enhance investment in clinical trial infrastructure in locations where resistance is currently prevalent, such as the Multi-Drug Resistant Organism (MDRO) Network, a collaboration within the US National Institutes of Health funded Antibacterial Resistance Leadership Group (ARLG). Another approach to increase participants is to conduct studies on multiple sites.[51] Pre-enrolment strategies such as early informed consent in patients at risk of resistant infections may also aid enrolment.

Superiority of drugs can be shown with few enrolled participants with resistant pathogens since death rates are higher. The ARLG recently conducted an observational study in around 140 patients that suggested improved mortality of a new antibiotic compared with an older antibiotic[52]; this finding might be confirmed in small randomised trials. As few as 24 patients would be needed for a well conducted trial of a new drug that decreases mortality with similar efficacy to the early trials of penicillin relative to placebo: if 9/12 patients survive with the new drug versus 4/12 with standard care that gives a P value of 0.03.[31]

In addition, large safety databases are not required when the benefit is improved survival in patients with no options. Superiority trials are also not subject to restrictions that lessen the feasibility of non-inferiority trials, such as standardised control drugs of known effectiveness, exclusion of patients taking previously effective therapies, and replication of design features of earlier studies.

The existence of effective therapies does not mean that we require non-inferiority trial designs. Superiority designs can use active controls. In randomised, blinded "add-on" superiority trials, new drugs are added to best standard therapy and compared with standard therapy plus placebo. This design is used in oncology, where drug resistance is also common.[53 54]

Superiority designs might also catalyse development of diagnostics to streamline trial enrolment, and appropriate patient selection and antibiotic use. Non-inferiority trials are a disincentive to develop appropriate diagnostics since inaccurate diagnosis can minimise differences between interventions, making non-inferiority more likely.[55]

We share concern about the growing need for more effective treatments for infectious diseases caused by multidrug resistant bacteria. But new treatments should show demonstrable benefits for patients, not just activity against organisms, and the goal of drug development should be to help both current and future patients. Regulators should therefore insist on properly designed, executed, and powered superiority trials in patients who lack any effective options and in whom the benefit-risk considerations are justifiable.

John H Powers, professor of clinical medicine, George Washington University School of Medicine, Washington, DC jpowers3@aol.com

Scott R Evans, senior research scientist, Department of Biostatistics and the Center for Biostatistics in AIDS Research, Harvard T H Chan School of Public Health, Boston, USA

Aaron S Kesselheim, associate professor of medicine, Program On Regulation, Therapeutics, And Law, Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Boston

Cite this as: *BMJ* 2018;360:k587

OBITUARY

Arnold Maran

Otolaryngologist who became known as the "Voice Doctor"

Arnold George Dominic Maran (b 1936; q Edinburgh 1959; FRCS Ed, MD Ed, FRCS Eng, FACS, FRCP Ed, FDS (Hons) RCS Ed, FCS (Hons) S Afr) died after a short illness on 10 December 2017

Arnold Maran will be remembered by many as the "Voice Doctor," a moniker he earned for his work optimising the vocal chords of singers and actors—and also of former president of Iraq Saddam Hussein. Maran liked the title so much that he used it in the title of his 2005 book, *The Voice Doctor: The Story of Singing*.

But Maran's voice work, which started in the late 1980s, came late in his career. His more important contribution to medicine started nearly 20 years earlier, when he helped pioneer surgery for head and neck cancer in the UK.

In 1972 Maran teamed up with fellow otolaryngologist Philip Stell (read obituary on bmj.com) to publish their popular and esteemed *Stell and Maran's Textbook of Head and Neck Surgery and Oncology*. An updated fifth edition of the book, with a foreword and an introduction written by Maran, was published in 2012.

In addition to his head and neck cancer work, Maran was a talented facial plastic surgeon and one of the pioneers of endoscopic sinus surgery. He also was a leader in the surgical community, serving as treasurer, secretary, and finally president from 1997 until 2000 of the Royal College of Surgeons of Edinburgh.

Italian heritage

Arnold George Dominic Maran was born on 16 June 1936 in Edinburgh to an Italian mother and a father who was second generation Italian. During the second world war—with the UK and Italy on opposing sides—young Arnold tried to conceal his Italian heritage.

In 1951, at the age of 15, Maran made his first trip to Italy and fell in love with the country. "It was 'la dolce vita,'" Arnold later said. "Such a contrast to postwar Britain."

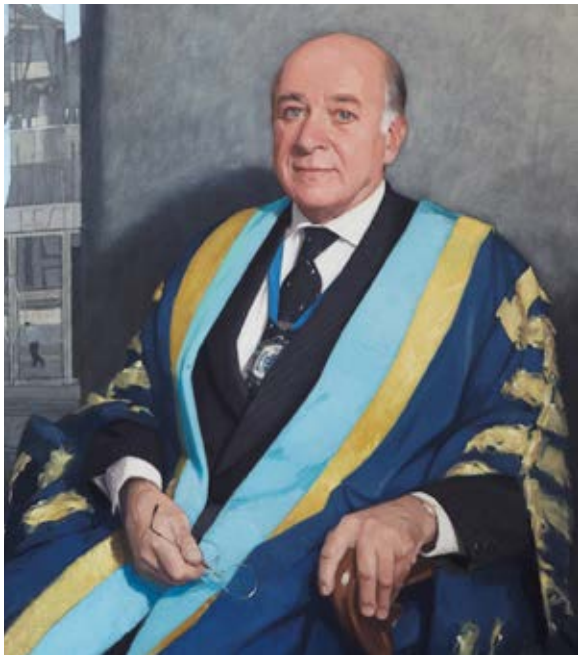
He studied medicine at Edinburgh University. After qualifying he trained in ear, nose, and throat medicine at Edinburgh's Royal Infirmary. In 1963 he became a fellow of the Royal College of Surgeons of Edinburgh, and a year later decided to leave his hometown.

He spent a year at the University of Iowa and then returned to Scotland for an appointment at the Royal Infirmary in Dundee. In 1967 he received his doctorate from Edinburgh. After six years in Dundee, he returned to the US for additional training, this time at the University of West Virginia, and in 1975 he became a fellow of the American College of Surgeons. He then returned to his hometown and was appointed consultant otolaryngologist. He joined the faculty of Edinburgh University, where he later was appointed the first professor of otolaryngology.

Edinburgh Voice Centre

In his spare time, Maran was involved in the Edinburgh music scene. He liked opera and also played piano in jazz bands. He heard about human voice research being done in Edinburgh by Colin Watson, an opera singer and recording engineer. Maran contacted Watson, and the two men founded the Edinburgh Voice Centre, one of the first voice clinics in the UK.

Maran believed that performing artists needed specialised medical care along the lines of sports medicine for athletes



Maran believed that performing artists needed specialised medical care along the lines of sports medicine for athletes. In 1998 he published a paper on the topic in the *British Journal of Sports Medicine*. He declined to name any singers treated at his voice clinic, but it is known that his patients included singers and actors who performed at the annual Edinburgh International Festival. One patient whom Maran did name publicly was Saddam Hussein, whose family physician was an Iranian man who had trained under Maran in Dundee. Maran made several trips to Iraq, and on one occasion examined Saddam for a hoarse throat.

After retiring in 2000, Maran divided his time between his homes in Orchard Brae in Edinburgh and the Umbria region of central Italy.

Maran held various leadership roles in professional bodies and won many prizes and medals. One of his most moving experiences, he once recalled, was visiting Mother Teresa at her hospice and orphanage in Calcutta in the early 1990s. "And this little Albanian woman said to me, 'You're very lucky to be a doctor. But you must remember, medicine is not a profession. Medicine is not a business. Medicine is a vocation.'"

Maran added: "I then thought I should stay there and lift people out the gutter and look after them. Then I came back home, went to the private hospital, took out tonsils, and sent an invoice. It made me feel so small. I regret I never did that work in India."

Maran leaves his wife, Anna, and two children.

Ned Stafford , Hamburg
ns@europefn.net

Cite this as: *BMJ* 2018;360:k437

POOR POLICY MAKING

"First, do no harm" is true for management too

McCartney is spot on about the reasons for the NHS crisis (No Holds Barred, 13 January). Huge amounts of money have been wasted on initiatives like the Care Quality Commission. But much worse is that unproven and time consuming ideas distract us from our day job.

We have been given extra work dealing with obesity, health checks, and the fallout from screening. None of this was part of our work in the past and no one has shown that we are effective at dealing with it. What work should we stop doing so that we can fit it all in our day?

Our managers are incompetent—or are they wasting so much time and energy dealing with the latest initiatives and firefighting cost pressures that they never focus on the main job?

"First, do no harm" applies as much to the management of the NHS as it does to medical practice.

Ted A Willis, GP, Brigg

Cite this as: *BMJ* 2018;360:k656

PRIORITISING NUTRITION

Dietitians' advice is evidence based

I agree with Womersley and Ripullone that medical students should have more nutrition education to become more effective at giving lifestyle advice (Personal View, 28 October).

But I disagree that "dietary interventions are considered to be outside of the evidence base, unscientifically 'fluffy,' and the domain of dietitians rather than doctors."

Dietitians give only advice that has an evidence base. They are regulated by law and, like doctors, are governed by an ethical code. Dietitians follow NICE's guidance, which for type 2 diabetes states that patients should be provided with individualised and ongoing nutritional advice from a healthcare professional with specific expertise and competencies in nutrition.

Understanding and respecting the roles of other healthcare professionals also seems to be lacking in medical training.

Until medical students do receive more nutrition training they should refer their patients to dietitians who can provide their patients with individualised, evidence based dietary advice.

Mary Hall, dietitian, Cambridge

Cite this as: *BMJ* 2018;360:k650

LETTER OF THE WEEK

Scottish contract ignores needs of rural GPs

GPs in Scotland have accepted a new contract (Seven Days in Medicine, 27 January), but the fundamental approach remains unchanged from every contract in the history of medicine—designed from the urban based top, with a system centred focus on planning. Resourcing remains defined by the system's imagined capacity rather than the real diverse needs of people and communities.

The Scottish GP Committee (above) acknowledges that formulas are poor at allocating resources across heterogeneous systems. But it touts the workload allocation formula, despite clear evidence and concerns from rural GPs that it rewards demand, not need.

The committee says that "no practice in Scotland will see any reduction in nationally agreed funding." In reality, frozen income translates into a loss with tax changes and inflation, especially with no recognition of the higher costs of core GP services in geographically or demographically challenging areas. Even the costs of a basic continuing professional development course sky rocket when adding ferries, fuel, flights, hotels, and extra cover.

Consider prospective partners—would you choose a practice with an income boost or income protection? The recruitment and retention gap will widen, making recruitment even harder.

From day one, this contract increases the risks for remote general practices and their communities. If not tackled now, many rural areas may lose their medical services before phase two emerges from the negotiating chambers.

Cathy Welch, GP, Isle of Arran

Cite this as: *BMJ* 2018;360:k762

TRIVALENT FLU VACCINE

Cross protection of circulating influenza B

Despite this year's trivalent flu vaccine not containing the circulating B Yamagata strain (This Week, 13 January), it could still provide some cross protection with the B/Victoria strain.

In the UK in the 2015-16 flu season, there was a mismatch between the influenza B component of the trivalent vaccine and the dominant type of circulating influenza B virus. But a good level of cross protection was seen against confirmed cases of influenza B, from the B/Victoria containing vaccine.

John S Bradley, NHS principal public health practitioner, Bronllys

Cite this as: *BMJ* 2018;360:k725

PRECLINICAL RESEARCH

Biotech may be more effective than academia

The BMJ reports on the handling of animal testing data for the MVA85A tuberculosis vaccine (Cover Story, 13 January). Another aspect to consider is the balance of medical research and development between academia and the biotechnology industry.

Historically, medical academic staff at universities focused on research, teaching, and patient care, whereas drug companies engaged in research and development with departments dedicated to preclinical research and clinical trials. Around the 1980s, this pattern changed dramatically, favouring translational research at universities, encouraged by governmental and charitable grant funding agencies.

The compulsory registration of preclinical and clinical data is demanding and expensive and might be implemented more effectively in biotech companies than in medical academia,

which needs to split its efforts with substantial teaching or clinical obligations.

Some shift back could be mutually beneficial—strengthening the fundamental research platform in academia while allocating public funding for lifesaving health targets to the biotech industry.

Juraj Ivanyi, honorary professor, London

Cite this as: *BMJ* 2018;360:k758

Misunderstanding the goals of animal research

Ritskes-Hoitinga and Wever misunderstand the central value of most animal experimentation (Editorial, 13 January). Medical research spans fundamental discovery to clinical validation. Human studies must meet high levels of proof, so can generally rigorously test only a single hypothesis. Most animal studies are designed to discover new biology, so they often test multiple hypotheses simultaneously.

Using the type of study design seen in human trials might occasionally be justified in animals, particularly when we know that the model is highly predictive of human responses. But at the start of the MVA85A trial we had no idea how well animals predicted human protection. We could second guess the decision to proceed on the basis of the animal results, but there was no yardstick.

There is substantial pressure to apply clinical trial criteria to animal research. Although well intentioned, this represents a fundamental misunderstanding of the goals and practice of using animal models.

Eric J Rubin, professor, Boston
Sarah M Fortune, professor, Boston

Cite this as: *BMJ* 2018;360:k759

PREPARE before you ARRIVE

Ritskes-Hoitinga and Wever discuss tools for raising standards of animal research (Editorial, 13 January). But better reporting does not improve the quality of an experiment that has already been performed. Systematic improvement of animal research must begin with better planning.

We have constructed a set of planning guidelines called PREPARE, based on our experiences over the past 30 years (https://norecopa.no/PREPARE). PREPARE contains many of the elements in reporting guidelines like ARRIVE, but emphasises additional matters that can affect the scientific validity of the research, health and safety, and animal welfare. It contains a checklist, which serves as a reminder of items that should be tackled before the study.

We hope that the debate on poor reproducibility will rotate towards planning of animal experiments. We are in danger of wasting time discussing the quality of the lock on the door of the stable, from which the horse has already bolted.

BELLE MELLOR

Adrian J Smith, secretary, Oslo
R Eddie Clutton, director, Easter Bush
Elliot Lilley, senior scientific officer, Horsham
Kristine E Aa Hansen, assistant professor, Oslo
Trond Brattelid, research adviser, Bergen

Cite this as: *BMJ* 2018;360:k760

RESPONSE

GMC chair's reply to Nick Ross's letter

Dear Nick,

I have read in full the court judgments and GMC decisions taken around the Bawa-Garba case and am keen to shed some light on our role in a law abiding and democratic society.

We acknowledge that concerns about manslaughter by gross negligence convictions, and this subsequent judgment, could make doctors less candid about errors and that this case has set us back in our aim to support doctors as the best way of protecting patients.

I agree entirely that to err is human, and I have certainly made mistakes as a doctor. But a conviction for gross negligence manslaughter is not about everyday mistakes—the failings must be exceptionally bad to result in a conviction after taking into account all mitigating factors. You may consider the law to be flawed, and it is your right to make representations about that. But the GMC cannot be above the law of the land.

We will lead a review to explore how the law of gross negligence manslaughter is applied to medical practice. Since 2016, I and others have discussed with the Health Secretary the creation of a "safe space" in healthcare and a form of legal privilege, akin to the airline industry, which you quote. But parliament has chosen not to enact that. Until it does, we remain bound by UK law as it stands.

On your specific request for a statement of our position, I wholeheartedly agree that protecting and promoting patient safety must be the first priority of the GMC and that candour is one crucial part of that. Retribution has no place in our work. The Medical Act 1983 sets out that our role is to protect the public. The legal systems of the UK are predominately adversarial in nature, and as a statutory body set out in UK law, we follow that law.

The GMC must remain willing to learn, but it cannot ignore the law or be swayed in its decision making by outcry from sections of the public when the views of the rest of the UK's 65 million citizens are unknown. In every one of the nine convictions for gross negligence manslaughter since 2004, having considered the facts in each case, and without regard to the seniority or ethnicity of the doctor concerned, the GMC has sought erasure.

The GMC was removed from decision making in individual fitness to practise decisions in 2004 in the wake of public disquiet around several bad doctors who harmed patients and were not dealt with by the system, and the GMC was seen as a doctors' club looking after its own. I cannot envisage a situation where the public would countenance a return to the profession deciding among itself on the fitness to practise of its colleagues. But I can confirm that I and the council have full confidence in how the registrar has taken such a difficult decision after full consideration of this case and the law.

Terence Stephenson, GMC chair, London

Cite this as: *BMJ* 2018;360:k765

Real Nick Ross's letter at bmj.com (*BMJ* 2018;360:k667)