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Francis report recommends a whistleblowing guardian in every NHS organisation(*BMJ* 2015;350:h828)

Whistleblowing in the NHS

Time for a public inquiry to tackle ongoing problems with bullying, intimidation, and reprisals

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Whistleblowing in the NHS is now a mainstream topic, thanks in part to two key reports published in the first three months of 2015: the Freedom to Speak Up review, chaired by Robert Francis, QC,[1] and Anthony Hooper's review into how cases involving whistleblowers are handled by the General Medical Council.[2] Despite these reports, and the interest and attention of the secretary of state for health, the health select committee, and the media, speaking up about patient safety remains both a duty and a huge personal risk—a "catch 22" situation for health professionals that cannot be allowed to continue. Raising concerns without fear is central to patient safety, and much remains to be done to make it happen.

The Freedom to Speak Up review is clear that the NHS has a serious problem. Francis writes: "I have concluded that there is a culture within many parts of the NHS which deters staff from raising serious and sensitive concerns and which not infrequently has negative consequences for those brave enough to raise them."

This conclusion was not reached lightly, but after consideration of a wealth of evidence from 612 individuals, 43 organisations, and a thematic review of over 400 of the individual responses. Francis met with several people who had raised concerns and then been badly treated, including vexatious referrals to the GMC and blacklisting from obtaining another NHS post.

My organisation (Patients First) made representations to both Francis and Hooper, in person and in writing. The representations to Francis reflected the experience of over 70 NHS whistleblowers.[3] It is clear that these experiences chimed with the wider evidence.

Neither review compelled any person or organisation to give evidence or respond to inquiry; neither review was commissioned to look in detail at individual cases, although both heard from many individuals. Yet both reviews reached authoritative conclusions and formulated recommendations for good practice. Employers must review their understanding of what a whistleblower is—it is anyone raising a concern—and action needs to be taken urgently to prevent the bullying that can (and often does) follow.

Employers must review their understanding of what a whistleblower is—it is anyone raising a concern

Francis found that the problem was widespread and systemic within the NHS: "I heard shocking accounts of the way some people have been treated when they have been brave enough to speak up . . . The number of people who wrote to the review who reported victimisation or fear of speaking up has no place in a well run, humane and patient centred service."

He also found that the law is weak and does not protect whistleblowers, something campaigners have been reporting for some time. However, by not calling for a public inquiry Francis has missed an opportunity to clear the air, ensure silenced voices are heard, and protect patients.

The recommendations of Francis's review need to be implemented in full to achieve what the best organisations are probably already doing. What remains a real concern, as exemplified by one person's submission,[1] is the lack of accountability and inconsistent intervention by health regulators. People are passed from place to place with raised expectations, only to be left high and dry after many weeks or even years of stress. Patient safety concerns are lost in the confusion.

Beware retaliation

The GMC (and other professional regulators) recognise the importance of speaking up to protect patient safety. All health professionals have a duty to do so. The fact that it remains risky and difficult is little short of scandalous.[1] The GMC has also consistently reported a culture of bullying when doctors try to speak up, and Hooper confirms that: "An employer might use the process of making an allegation to the GMC about a doctor's fitness to practise as an act of retaliation against a doctor because he or she raised concerns, or, simply, as an inappropriate alternative to dealing with the matter in-house."

As his report recognises, the prospective loss of a career is a particularly harsh consequence for a doctor willing to speak up to protect patients.

"Since the main objective of the GMC is to protect, promote, and maintain the health and safety of the public,"[4] the Hooper report recommends that if a doctor has raised a concern this will be "material, if not highly material" to any examination of his or her fitness to practise. Hooper's recommendations are largely directed at referrals from health employers, including NHS trusts. He urges the GMC to be cautious in the early stages of these referrals and recommends effort is made to ensure they are not reprisals.

This might include looking at any concerns that have been raised about patient safety by the doctor involved, and establishing a clear timeline of events to put any organisational referrals into their proper context. He also recommends that referrals are supported by a statement of truth declaring that the facts are genuine. His recommendations are welcome and should be implemented.

The Freedom to Speak Up review offers models of good practice for employers and agrees with campaigners that victimisation of whistleblowers is widespread. Furthermore, whistleblowers must navigate a bewildering, complex, and unaccountable system to make their disclosures. When they need protection it just isn't there.

The Hooper review is a welcome acknowledgment that something is not right within the GMC. These reviews underline how much more needs to be done and how the broader health and legal systems need reform. Only a public inquiry can reveal the systemic failings and the underlying reasons that have led to such a damaging and defensive culture within the NHS.

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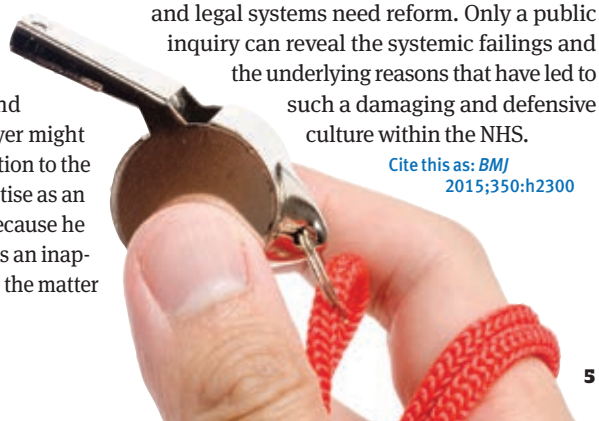

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- Investigation and treatment of imported malaria in non-endemic countries (*BMJ* 2013; 346: f2900)
- Overdiagnosis and mistreatment of malaria among febrile patients at primary healthcare level in Afghanistan (*BMJ* 2012; 349: e4389)
- Imported malaria and high risk groups: observational study using UK surveillance data 1987-2006 (*BMJ* 2008; 337: a120)

Plasmodium vivax malaria in the UK

New insights into an old enemy

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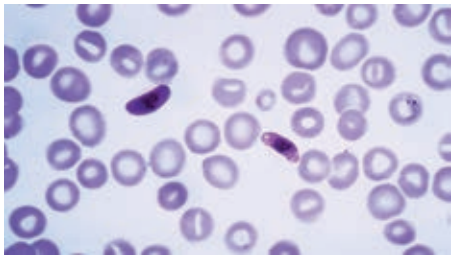
Plasmodium falciparum malaria is so lethal and ubiquitous that one could easily forget that other species of malaria are globally important too. In particular, *Plasmodium vivax*, the main cause of relapsing malaria, affects up to 300 million people annually, and occurs in far wider and ecologically diverse settings than *P falciparum*.

Yet *P vivax* remains seriously understudied. Today, querying "*Plasmodium falciparum*" on PubMed generated 31 493 citations compared with only 6520 for "*Plasmodium vivax*." Recent data suggest that the epidemiology of *P vivax* may be shifting[1 2] and that the parasite could be growing more virulent.[3 4] But the evidence supporting these rests largely on small, cross sectional studies with limited geographical scope. Without large, systematically collected, geographically diverse, longitudinal datasets, we cannot be certain that these trends are for real, let alone try to explain them based on external forces, such as global warming or urbanisation.

In this context, the linked paper by Broderick and colleagues is well timed.[5] These authors analysed 27 years of data and over 50 000 clinical samples collected by the Public Health England Malaria Reference Laboratory. To enter the laboratory's dataset, samples had to be confirmed either by smear microscopy, histology, or polymerase chain reaction, making this dataset particularly robust. Moreover, the laboratory had resources enabling it to link malaria cases back to the reporting clinicians, so as to capture additional information on timing of exposure, clinical outcomes, travel destinations, and the use of chemoprophylaxis during travel.

Interrogating the local

It may seem counterintuitive to study *P vivax* globally by analysing data from the United Kingdom, but there are good reasons for doing this. Firstly, the UK is ethnically diverse, with many citizens tracing their roots to Africa and South Asia, places where *P vivax* is common. Secondly, because malaria has been eliminated from the UK, all such cases are, by definition, acquired by travelling somewhere else. Also, having largely grown up in the UK, many or most UK travellers of African or Asian descent lack (or have lost) natural immunity to malaria. This enables cleaner inferences to be made about the epidemiology and biology of the parasite in ways that, paradoxically, would be harder to do among people living in malaria endemic zones.



Not rare and not benign

Several interesting observations emerged from Broderick and colleagues' analysis.

P vivax comprises a surprisingly large proportion of malaria in the UK: roughly 25% of cases had *P vivax* malaria (12 769). This is not a rare disease. General practitioners should be proactive in seeking vivax malaria in returning travellers with fever, particularly as *P vivax* is harder to detect on blood smears than *P falciparum*, and symptoms may take months to appear after leaving a malarial zone.

Secondly, the distribution of *P vivax* and *P falciparum* cases in the UK varies substantially by geographical region. *P falciparum* was clustered in London (attributed to a larger concentration of people with west African heritage), whereas *P vivax* was more common in the north west and Yorkshire (reflecting a greater concentration of people with South Asian heritage).

Thirdly, although *P vivax* was about one tenth as lethal as *P falciparum*, all deaths due to *P vivax* occurred among older adults (median age 72 years). This is a stark reminder that "benign" tertian malaria is a misnomer: *P vivax* is only benign relative to *P falciparum*.[6]

Fourthly, despite a steady increase in travellers to malaria endemic areas, the incidence of *P vivax* in the UK has actually declined sharply. We do not yet know whether this favourable trend is the result of better adherence to chemoprophylaxis or a real decline in malaria incidence in source countries. This is a critical question for future research.

Arguably most interesting are Broderick and colleagues' data on seasonal incidence. They sorted *P vivax* cases according to source region (African or South Asian), and also by calendar month, allowing the authors to explore the relations between malaria transmission, season, weather, and geography.

Predictably, in West Africa, where the climate is perennially hot and humid, monthly *P vivax* rates in travellers were stable over time. By contrast, in South Asia *P vivax* was concentrated around the monsoon rains.

More surprising was that the duration of latency was strongly influenced by the month in which the traveller returned to the UK. Unlike other plasmodium species, *P vivax* and *Plasmodium ovale* can remain latent in liver cells, emerging months after infection to invade and replicate within red cells and trigger clinical disease. We have known for decades that the duration of *P vivax* latency gets longer the further north travelled from the equator. It has been theorised that this is an evolutionary adaptation that enables *P vivax* to wait out the winter months, timing its entry into the bloodstream until the warm summer months, when vectors such as mosquitoes are again on the wing.[7]

Monsoons bring rain to South Asia from June to August. Latency among the South Asian travellers was shortest among those returning between March and August (the wet months) and longest among those returning between October and February (the dry months). Since the goal of a malaria parasite is to maximise opportunities for getting back into a mosquito, delaying entry into the bloodstream until the season when mosquitoes are plentiful seems a very pragmatic adaptation. Although the link between latency of imported malaria and season has been noted before, Broderick and colleagues' novel approach was to examine latency in relation to the weather in the source country where the parasite was acquired, rather than the local weather in the UK, as had been observed previously.[8] This makes their findings all the more compelling and provides a clear illustration of how marvellous, complex, and powerful are the forces of evolution.

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RESEARCH, p 9

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Bioethicist Udo Schüklenk described the aid organisations as "a mixed bunch of Christian missionaries busily trying to get their hands on the last available experimental agents while on private medical jets out of west Africa

Ebola and ethics: autopsy of a failure

Thousands died while we argued over the wrong questions

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The current epidemic of Ebola virus disease has attracted medical ethics commentators like bees to a honey pot. No previous infectious disease epidemic has elicited such a flurry of articles on the ethical challenges associated with infection control and treatment in such a short time. Has this been of any use?

The ethical questions raised by various authors broadly fall into three categories. The first relates to questions of individual medical ethics, in particular surrounding the compassionate use of experimental drugs and vaccines. The second concerns allocation of resources to these experimental treatments versus infection control. And the third centres on how resources should be spent in the long term—on building a public health and clinical infrastructure that can cope in an epidemic instead of propping up a weak infrastructure during a humanitarian crisis.

The tension between these moral challenges can be grouped along two axes: individual versus public health, and short term versus long term (figure).

The short term use of experimental drugs such as ZMapp, first used in a few repatriated health workers from high income countries, attracted far more public attention than it deserved. It generated a series of ethical questions that are hard to answer and distracted from the real, practical, and urgent business of controlling the wider Ebola epidemic. Commentators argued about whether randomised trials were required in the heat of the epidemic, the level of personal risk that might be acceptable for recipients, who should receive these drugs, how to ensure informed consent, and whether health professionals should get preferential treatment, among other things.

The inappropriate focus on experimental treatments for individuals diverted attention away from infection control and other measures that would benefit everyone. In August 2014, Médecins Sans Frontières (MSF) was the first to point out that the international response to the epidemic was "dangerously inadequate."[1] International collective action came too late, and too little was done.[2] MSF called for support in the form of laboratory staff, healthcare workers to provide supportive care, and portable equipment to isolate patients.[1]

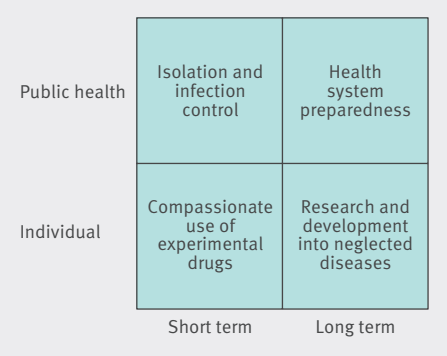
Only a few writers have commented on the ethical aspects of a misguided international effort. Bioethicist Udo Schüklenk characterised the humanitarian intervention as a theatrical farce. He described the aid organisations as "a mixed bunch of Christian missionaries busily trying to get their hands on the last available experimental agents while on private medical jets out of west Africa."[3] He also criticised WHO's recommendations to provide access to experimental drugs as "pointless grandstanding in the face of a pandemic that requires a public health response."[3] David Heymann, an infectious disease epidemiologist, prioritised stopping the outbreak using intensified patient isolation, contact tracing, and community empowerment flanked by properly conducted clinical trials of treatments such as survivor serum.[4]

In November 2014, Annette Rid and Ezekiel Emanuel published a viewpoint that rightly stressed the need to prioritise strengthening of health systems over experimental treatments because the treatments are unlikely to have a noticeable effect on the epidemic, even if effective.[5] Jacob and colleagues wanted effort directed at patient outcomes instead.[6] These arguments show why a clear distinction is needed between short and long term responses, and between the needs of individuals versus the wider public health. Where Rid and Emanuel think big picture and long term, Jacob and colleagues think about the needs of individuals, in the short term. Both are important, and they should not compete.

What went wrong?

In my view, the expert meeting on experimental drugs and vaccines convened by WHO in August 2014[7] not only sidetracked relief efforts but led medical ethicists from all over the world sheepishly down the wrong path. The moral challenges surrounding the compassionate use of experimental drugs and vaccines are complex. Heated debate arose, and the wider public health perspective was lost in the noise. The misguided WHO expert panel and relief effort was picked up by some medical ethicists.[3 5 8] However, their insights came too late to change the course of events or the public debate.

What can we learn from this failure? Governments, international organisations, and donor agencies need to take a wider perspective and a longer term view on health system preparedness when it comes to effective prevention of epidemics, including Ebola.



Once an epidemic occurs, rapid deployment of proved methods of infection control should take precedence over experimental treatments. In the wake of the 2009 H1N1 influenza pandemic a WHO review committee recommended the creation of a $100m (£67m; €93m) contingency fund to allow rapid responses to future pandemic threats. This recommendation was ignored, which partly explains the delayed and fractured response to the Ebola epidemic.[9]

A renewed focus on developing more effective drugs and vaccines against neglected tropical diseases is another important long term measure that should happen now, between epidemics.[10]

The World Bank estimates that the two year socioeconomic effect of the current Ebola epidemic could reach $32.6bn.[11] If only a fraction of this amount had been spent on health system preparedness before the current epidemic, early case identification and containment, contact tracing, and supportive care for the few people affected in the first wave of the disease would have been possible. Many of the more than 10 000 deaths reported by 17 April 2015 might have been prevented.[12] Finally, the benefits of a well prepared health system would extend to many other diseases, including HIV/AIDS, tuberculosis, and malaria.

Medical ethics can provide useful insights for decision making in epidemics, provided that you ask the right questions.

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FEATURE, p 16

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The 71 drugs approved by the FDA from 2002 to 2014 for solid tumours have resulted in median gains in overall survival of only 2.1 months

Why do cancer drugs get such an easy ride?

Rushed approvals result in a poor deal for both patients and cancer research

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Unlike most other diseases, cancer instils a special fear and "is treated as an evil, invincible predator, not just a disease."[1] The ability of drug companies to charge very high prices, even when most approved cancer drugs provide little gain for patients, drives much of the research, as desperate patients lead some governments and private insurers to pay whatever companies charge. Officials within the US Food and Drug Administration are enthusiastic about new cancer drugs. Richard Pazdur, who oversees oncology activities for the FDA says that new cancer drugs are so effective that "We don't have a lot of questions on [these] drugs because they're slam dunks. It's not if we're going to approve them. It's how fast we're going to approve them."[2]

The methodological weaknesses in oncology trials do not support such enthusiasm. Researchers compared 8942 oncology clinical trials conducted between 2007 and 2010 with trials for other diseases.[3] Trials for cancer drugs were 2.8 times more likely not to be randomised, 2.6 times more likely not to use a comparator (single arm), and 1.8 times more likely not to be blinded. Each undermines the validity of outcomes but reflects what regulators will allow.

Less valid trials reflect an easy ride from regulators for drugs that usually offer few significant benefits for patients. A review of drugs for solid cancers approved by the European Medicines Agency (EMA) in its first 10 years found that, overall, new oncology drugs improved survival by a mean and median of 1.5 and 1.2 months, respectively.[4] The 71 drugs approved by the FDA from 2002 to 2014 for solid tumours have resulted in median gains in progression-free and overall survival of only 2.5 and 2.1 months, respectively.[5] Further, only 42% met criteria set by the American Society of Clinical Oncology Cancer Research Committee for meaningful results for patients.[6]

Accelerated approval and surrogate outcomes

A second easy ride comes from regulators creating more ways to shorten review times.[7] In

Europe between 1999 and 2009, oncology drugs were the class that was most likely to be approved through an accelerated pathway.[8] Priority approval shortens the FDA review time from the standard 300 days to 180 days, but the two processes are supposed to be equivalent. In practice, postmarketing label changes are substantially more common for oncology drugs approved by priority review than for those subject to standard reviews, suggesting possible deficiencies in the priority review evaluation.[9]

Cancer drugs approved using early stage evidence had "a 72% greater odds of serious adverse events occurring in their pivotal trials than did cancer drugs that were approved with more rigorous studies."[7] Once drugs are available, even if they subsequently prove to be ineffective, withdrawing them can be a lengthy process and generates substantial opposition, as the case of bevacizumab for metastatic breast cancer demonstrates.[7]

A third easy ride comes from European and US regulators allowing companies to test cancer drugs using surrogate measures instead of survival and other patient centred measures. The three most commonly used surrogate endpoints all use radiological measurement of tumour size as evidence of benefit, even though the exact date of tumour progression can never be precisely known from these measurements.[10]

Surrogate endpoints are highly variable in their ability to predict overall survival.[11-13] A review by the German Institute for Quality and Efficiency in Health Care concluded that the validity of tumour response measures as surrogates for patient relevant endpoints in colon and breast cancer remains unclear.[14] Despite these limitations drug companies are eager to use surrogate endpoints because the trials require fewer patients and can be completed faster and more cheaply than trials that test for survival. The FDA and EMA find them acceptable and base most of their approvals on them.

The FDA used surrogate endpoints to approve 68% (39/57) of oncology drugs processed through the standard approval pathway and for all 14 applications granted accelerated approval from January 1990 to November 2002.[15] In Europe, from January 1995 to December 2004, most cancer medicines were approved on the basis of surrogate endpoints such as "tumour shrinkage [that] did not translate most of the time into significant survival benefit."[4]

In 2013, over 100 oncologists protested against the high prices charged for cancer drugs, when 11 out of 12 approved in 2012 provided only small benefits to patients.[16 17] The easy ride syndrome and lowering the efficacy bar encourage "the pursuit of marginal outcomes and a me-too mentality evidenced by the duplication of effort and redundant pharmaceutical pipelines."[5 18] Beyond cancer drugs, low bars for approval are why 90% of new drugs that companies develop are judged to add few or no clinical advantages over existing ones and yet have substantial risks of serious adverse events.[19 20] Easy ride regulators serve both patients and research badly.

A few changes could greatly improve the quality of cancer drugs and research. Leaders of Italy's Mario Negri Institute have long advocated a coherent model for the development, regulation, and use of better medicines.[21] They see no reason why regulators cannot insist on randomisation, improved overall survival, and phase III trials since good results in phase II are often not persuasive.[4] Patients and their doctors need to insist that regulators, established to protect the public, should require clear evidence that new drugs are clinically effective, based whenever possible on trials that compare them to current effective therapy using designs that are methodologically rigorous.

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