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Antibiotic drug research and development

Should it be funded through public-private partnerships to succeed?

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Two linked articles highlight two very good reasons for international health authorities and governments to be seriously worried about the emergence of antimicrobial resistance: the worldwide spread of multidrug resistant bacterial strains and the paucity of antibacterial compounds currently being researched.[1 2]

As antimicrobial resistance spreads worldwide and increasingly affects patients with very little buying power, traditional market forces will no longer provide the antibiotics that the world badly needs. The World Health Organization recently published a thoughtful analysis of the situation, along with measures that should be taken to face the threat.[3] However, no clear way of increasing new antibiotic research and development has emerged.

The development of antibiotics has been increasingly challenging in recent years. Despite tremendous advances in the biological sciences, the difficulty in identifying new mechanisms to kill human bacterial pathogens has discouraged the few companies that are still active in the field. Clearly, we can no longer rely on direct competition between private companies alone to drive the emergence of new drugs.

So and colleagues propose sharing the risks of the antibiotic drug development process by spreading the burden across all stakeholders, from academia to the private sector, as a potential answer to the current crisis.[2] Such broad sharing of resources, competences, and information should promote innovative approaches and a paradigm shift away from conventional methods of identifying antibacterial agents (via standard "Petri dish" assays or target based approaches) to exploring new ways to fight bacterial infections, such as by working on host-pathogen interactions, disrupting bacterial adaptability to the human host, or targeting latent bacteria. Microbiologists and clinicians, many of whom still take the view that "a good bug is a dead bug," may be challenged, as will regulators who will have to move out of their "confidence zone." However, past failure shows that we urgently need to step outside of traditional approaches.

Several "push" and "pull" mechanisms have been proposed to incentivise the private sector to invest in antibiotic development in response to the obvious failure of market forces to do so. However, such mechanisms alone are unlikely to incentivise drug companies to commit to the large investments needed to develop a new antibiotic, given the high risks of failure and the small return on investment.

Pull mechanisms, such as the bill to be presented to the US State Congress known as GAIN (Generating Antibiotic Incentives Now) can even be deleterious in the long term. This bill proposes to grant extended data exclusivity to companies that bring new antibiotics to market, as well as to prompt the Food and Drug Administration to review its guidelines for clinical trials of antibiotics. If the last measure is justified and needed, then extended market protection unfortunately goes in the wrong direction. Such actions would further strengthen the link between sales and revenues, a key factor that underpins aggressive promotion of a new antibiotic and its inevitable misuse. The bill does not provide guidelines on pricing (with consideration of the accessibility of new drugs in developing countries) or on the conservation (limited use) of any new antibiotic. Moreover, the proposed mechanisms are unlikely to motivate the private sector, given the still modest pricing of antibiotics compared with drugs directed at chronic and lifestyle diseases.[4]

In contrast, push mechanisms such as research grants, subsidies, dedicated funds, and tax credits can be helpful in the early discovery stage. They will not, however, stimulate necessary translational research and clinical development unless strong additional mechanisms are put in place to ensure drug development.

If the private sector is ill equipped to take up the challenge for economic reasons and the anti-infective community reluctant to embrace innovative approaches, who will develop the next generations of antibiotics? We must continue to invest heavily in research to ensure a renewable pipeline of products because any new antibiotic may eventually become obsolete. The market life of antibiotics is often short as bacteria become resistant despite preventive measures. It is thus reasonable that antibiotic development should be the responsibility of the public sector. Such a responsibility would mean that new antibiotics, the necessary tools to fight antimicrobial resistance in the long term, might be regarded as public goods. New antibiotics would then benefit not only a fortunate few but might be made available to every patient in need, whether from developed or developing countries, at an affordable price. The public sector could share the risks of drug development through funding, as suggested by So and colleagues,[2] and also the reward for success: bringing affordable antibiotics to the population.

Strong financial support for drug research and development from the public sector is key to driving true innovation because it would delink investment from the need to deliver financial returns, which is impossible in the private sector. Some have suggested the creation of an "International Fund for Antibiotic Research" financed by governments (in the model of the Global Fund), and coordination of research and development by product development partnerships. Such partnerships have been successful in developing new treatments for neglected tropical diseases, substituting efficiently for the private sector where market incentives have not driven research and development, and at very low costs. For example, the Drugs for Neglected Diseases initiative developed five new treatments for malaria, sleeping sickness, leishmaniasis, and Chagas' disease over seven years, with about €100m (£83m; $131m). Other partnerships, such as the Medicines for Malaria Venture, have also delivered innovative products in a cost efficient manner. Product development partnerships could provide a realistic way to engage into innovative antibacterial research and development by coordinating the resources, skills, and efforts of all current players (from academia to drug companies) while absorbing the risks inherent in drug development. Eventually, industry could be responsible for manufacturing and distributing the products, at a price that ensures the sustainability of production and distribution but that does not include research and development costs, which will have been financed through the public sector.

The battle against antimicrobial resistance requires innovative approaches, because new resistance will continuously emerge, and sustained efforts are needed to produce new antibiotics, to control their usage, and to ensure that every patient will have access to these life saving drugs.

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ANALYSIS, pp 22, 25

A threshold reduction from 0.20 ng/ml to 0.05 ng/ml led to significant reductions in event rates when attending doctors were informed of the assay results and were able to modify management strategies accordingly

doc to doc
An unusual cause of myocardial infarction
http://bit.ly/HjEfBB

New guidance for troponin assays

Drives down diagnostic thresholds in acute myocardial infarction

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ANTONIA REEVE/SPL

The diagnosis of acute myocardial infarction in patients with suspected acute coronary syndromes requires documentation of changing troponin concentrations in the first 24 hours, with at least one value being above the diagnostic threshold.[1] Although high sensitivity troponin assays have recently enabled the diagnostic threshold to be reduced, new guidance from the biochemistry group of the Global Task Force for the Universal Definition of Myocardial Infarction raises the prospect of further reductions.[2] The guidance recommends that the 99th centile value for plasma troponin is adopted irrespective of assay imprecision, whereas an assay coefficient of variation of 10% or less was mandated previously. In the linked study, Mills and colleagues examined the potential clinical impact of this new guidance in a cohort of patients with suspected acute coronary syndromes.[3]

The study's main finding was that application of the new guidance increased the proportion of patients diagnosed with myocardial infarction. This was a predictable consequence, but the increase was surprisingly large, with potentially huge implications for management. The authors estimated that application of the guidance would increase the number of patients diagnosed with acute myocardial infarction in the United Kingdom by 42 000 a year. The first question that arises, therefore, is whether this increase in clinical load would be rewarded by management decisions that improve patient outcomes. As the authors acknowledge, this question cannot be answered directly because the analysis was retrospective, and the high sensitivity troponin assay threshold of 0.05 ng/ml was used to guide diagnostic and management decisions. Moreover, there is no evidence base to draw on, because patients captured by the new low troponin threshold in the 0.012-0.049 ng/ml range have not been the subject of treatment trials.

The increased rate of diagnosis of acute myocardial infarction consequent on the new guidance is important for another reason. The rate of death or recurrent myocardial infarction at one year increased progressively with troponin concentrations above the 99th centile and was 13% in patients with concentrations in the range 0.012-0.049 ng/ml, who, before the new guidance, would have escaped a diagnosis of myocardial infarction. Thus, the new guidance recommending that the 99th centile value for plasma troponin be adopted as the diagnostic threshold, regardless of assay imprecision, would not only increase the infarct population but would also capture more patients at risk of recurrent events without increasing our ability to identify them (positive and negative predictive values of the high sensitivity troponin assay for the primary outcome hardly changed). The GRACE score, however, seems to retain high discriminatory value for mortality in acute coronary syndromes diagnosed by the high sensitivity troponin assay, although its performance at the diagnostic thresholds called for by the new guidance has not been assessed.[4]

High sensitivity troponin assays are useful for ruling out myocardial infarction early after presentation, often as part of a panel of biomarkers, although they seem to be just as effective on their own.[5 6] The authors' earlier study, in which a threshold reduction from 0.20 ng/ml to 0.05 ng/ml led to significant reductions in event rates when attending doctors were informed of the assay results and were able to modify management strategies accordingly, also provides evidence that lowering diagnostic thresholds for myocardial infarction may be beneficial.[7] However, there is no guarantee that the new recommendations will produce parallel improvements in patient outcomes. Simply reclassifying a subset of patients with troponin negative acute coronary syndromes to troponin positive myocardial infarctions will not change recommendations for lifestyle adjustment and secondary preventive treatment, which together represent the cornerstone of evidence based management in this group.

Mills and colleagues state that the new guidance could increase the number of patients referred for inpatient coronary angiography by 42%, but this may be an overestimate because there is little evidence that routine invasive management would improve prognosis in those troponin negative patients who would be reclassified as troponin positive.[8] The potential downside of the new guidance, therefore, is that it will further stimulate the culture of uncritical management responses to troponin positivity, and that many low risk patients will have little to gain and more to lose from the procedures that they will undergo. It is important, therefore, to emphasise the main conclusion of the linked paper that prospective trials are now needed to determine whether established treatment protocols for acute myocardial infarction will improve clinical outcomes in those patients reclassified by the new guidance.

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RESEARCH, p 14

Response on bmj.com "If we know that 5 million adults in the UK lack functional literacy, continuing the dissemination of health information primarily through written means may not be the most effective strategy. Is it time to consider alternative means of communicating information about health and health systems?" Maurice Joseph Bonar, psychiatrist, Dublin, Ireland

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How would you improve patients' health literacy?
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Health literacy

Is it time to shift our focus from patient to provider?

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Increasing people's ability to understand and engage in their healthcare is an international priority. Research, particularly from the United States, has shown that people who lack such ability have poorer health outcomes and increased mortality.[1] In the linked study, Bostock and colleagues show an adverse effect on mortality in patients in the United Kingdom too.[2] The findings of this study are worrying, but not surprising. The study also suggests that a third of older people in the UK have difficulty reading and understanding basic health information. Considered alongside data from the US and Australia,[3 4] these findings suggest that between a third and half of people in developed countries have difficulty understanding and engaging in their healthcare and that this has important consequences for health. In light of such findings it seems remarkable that the matter is not given higher priority.

The ability to read and understand health information has been characterised over the past 20-30 years as "health literacy," with the focus simply being on whether people could read and understand information, but the term has now developed a much wider scope. It now encompasses clinical risk (which focuses on screening for low literacy and leads to changes in clinical practice) and personal asset (aimed at developing skills that enable people to take more control over their health).[5] This means that there are three aspects to what is still called health literacy—the ability to read and understand health information; a wider ability to engage with the healthcare process; and the removal by healthcare systems of unnecessary complexity and barriers to patient understanding and involvement.

How can people who need easy to understand information and simplified health services be identified? Much research has focused on the evaluation of screening tools. However, because a third to half of people have difficulties, it seems sensible to offer the same accessible information and services to all patients,[6] especially as everybody could benefit from clearer health information and health systems that are easier to access. This would include using plain language, both oral and written, when communicating health information; using clear design in written materials for patients, which are often overly complex[7]; and rigorously user testing information with patients.[8] Such user testing is now used routinely for leaflets supplied with drugs across the European Union.[9] For clinicians who communicate information to patients there is widespread support for specific methods that help to confirm understanding, such as Teach Back (which checks how clearly the professional has communicated and how well the listener has understood),[6] and more general support for health professionals to develop their communication skills.

The ability of patients to understand and access healthcare…is a two way street…health professionals [should] consider how they can change the health information and health systems they offer, to make them as easy to understand and interact with as possible

LIFE IN VIEW/SPL

An explicit goal of the drive to increase health literacy is to improve health outcomes. However, empowered and informed patients may make decisions that they consider to be right for them, but which are not what their health professionals consider to be the right course. An informed and engaged patient is not necessarily an obedient patient. For example, in a randomised controlled trial, a decision aid increased levels of knowledge and informed choice but resulted in a lower participation rate in screening for bowel cancer.[5]

How is policy changing to reflect what is now known about the importance of health literacy? In the US, a recent national action plan moved the spotlight towards how services are provided, with a focus on removing barriers.[7] This is reinforced by provisions in the Affordable Care Act and the Plain Writing Act.[10] In addition, a health literacy "universal precautions toolkit" is being evaluated in the US.[11] In the UK, despite government proposals for more understandable information, together with involvement and engagement of patients, specific actions have not yet been identified.[12] Interestingly, the UK proposals do not use the term health literacy, and the widespread use of this term by others may be one of the reasons why more progress has not been made. There are many definitions of health literacy, and many stakeholders continue to understand the term only in its literal sense. Health competence has been suggested as an alternative term, but, in this of all situations, a more patient friendly term is needed. Most definitions encompass the notion of patients' capacity or ability, so an alternative term might be health ability. The right terminology matters when it comes to getting professionals and patients on board.

The ability of patients to understand and access healthcare depends on both engagement and communication. It is a two way street, with one important focus being a wider drive to improve people's abilities. However, most health professionals and health managers cannot achieve this in their day to day work. What they can do is to consider how they can change the health information and health systems they offer, to make them as easy to understand and interact with as possible. Future research should focus on evaluating attempts by professionals and health systems to remove barriers to understanding and engagement for all patients.

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RESEARCH, p 15

Authors of trials and systematic reviews… should report the rationale for conducting subgroup analyses and specify planned subgroup analyses in study protocols, including the predicted direction of the difference

Subgroup analyses

The devil is in the interpretation

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Sun and colleagues found, in the linked systematic review, that about a third of a representative sample of recent randomised trials published in core clinical journals report subgroup analyses.[1] After judging these reports of subgroup analyses using 10 carefully developed predefined criteria, the authors conclude that only in very few instances can we be confident that subgroup analyses provide a better estimate of effect than the overall results of trials, and they describe in detail the reasons why. These findings are consistent with what could be expected on the basis of previous reviews and the play of chance.[2-7]

Previous reviews of published trials and protocols have found that subgroup analyses are commonly reported (38-87% of the time),[2-7] and that appropriate statistical analyses (tests of interaction) are not used 38-91% of the time.[2-5] In addition, planned subgroup analyses are commonly not reported (48-69% of the time) and 43-91% of randomised trials report subgroup analyses that were not planned.[6 7] When subgroup analyses are reported, authors claim differences in 25-69% of cases, and these results are commonly featured prominently (15-45% of the time).[2-5]

The extent to which the consistency of subgroup findings across trials can be assessed is limited by authors' failure to interpret their results in the context of a systematic review of other trials.[8]

In 1983 the authors of a paper that presented 146 subgroup analyses of the Beta Blocker Heart Attack trial, found, unsurprisingly, that the results were normally distributed. Roughly 2.5% of the subgroup analyses had results that were "significantly" worse and 2.5% had results that were "significantly" better.[9] Five years later the International Study of Infarct Survival 2 (ISIS-2) trial found that aspirin reduced mortality after heart attack overall (P<0.00001) but increased mortality by a small amount in patients born under Gemini and Libra astrological signs.[10] Six years after that, the DICE (Don't Ignore Chance Effects) collaborators in their meta-analysis of trials of DICE therapy (rolling dice) for acute stroke found that red dice are deadly, on the basis of a predefined subgroup analysis by colour of dice.[11] All of these findings illustrate the important message that chance influences the results of clinical trials and systematic reviews of trials. Unfortunately, both researchers and clinicians can easily be misled by the play of chance.

Sun and colleagues' findings provide a clear indication of the extent to which subgroup analyses are undertaken, reported, and interpreted uncritically. This has important implications for researchers, authors of systematic reviews, editors, clinicians, and patients.

There are many compelling reasons for performing subgroup analyses, but the interpretation of their findings can be challenging. Authors of trials and systematic reviews can help by limiting the number of subgroup analyses that are conducted to those with a clear prespecified rationale. They should report the rationale for conducting each subgroup analysis and specify planned subgroup analyses in study protocols, including the predicted direction of the difference. Appropriate statistical analyses should be used.

Editors can improve the situation by requiring that authors report and interpret subgroup analyses appropriately in trials and systematic reviews. Requirements should include clear and comprehensive reporting of all subgroup analyses and the extent to which criteria for evaluating the credibility of each subgroup analysis were met, and the use of language that reflects the extent to which such criteria were met. The box provides examples of appropriate language for reporting.

Clinicians and patients should, as a rule, base decisions about treatments on systematic reviews of trials and not on single trials, unless no other relevant trials exist.[8] Decisions based on poorly interpreted subgroup analyses might result in effective treatments being withheld from some patients who would benefit.[12] They might also lead to the use of ineffective or harmful treatments in some patients. In the absence of a critically interpreted subgroup analysis for which a high degree of confidence is warranted, the best estimate of effect for a subgroup is the overall effect.

Sun and colleagues' 10 criteria are useful for assessing how much confidence to place in the results of subgroup analyses and when to base a decision on a subgroup analysis rather than on the overall results. To save time, however, a simple rule of thumb could be to first ask: "Are the results of the subgroup analysis and the overall analysis different enough that they would lead to different decisions?" If the answer is no, the detailed criteria do not need to be applied.

Examples of plain language that reflects how much confidence can be placed in subgroup analyses

Very low confidence: If important criteria are not met (for example, inconsistent subgroup effects across trials that have no compelling explanation or a high probability that the apparent subgroup effect occurred by chance) report the difference in effects as a hypothesis that warrants further investigation and do not include it in the abstract or conclusions ("The difference in effect is uncertain")

Low confidence: If differences in effects probably did not occur by chance, but the estimated subgroup effect warrants low confidence because other criteria were not met, report the subgroup effect as a hypothesis and do not include it in the abstract or conclusions ("There may be a difference in effect")

Moderate confidence: If most of the criteria are met and there probably is an important subgroup effect, report it as probable ("There probably is a difference in effect")

High confidence: If all or nearly all of the criteria are met and a high degree of confidence is warranted, report it without qualification ("There is a difference in effect")

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RESEARCH, p 16

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- Diagnosis and management of transient ischaemic attack and ischaemic stroke in the acute phase (*BMJ* 2011;342:d1938)
- Post-acute care and secondary prevention after ischaemic stroke (*BMJ* 2011;342:d2083)

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Discuss in BMJ Group's Stroke Medicine forum http://bit.ly/oJZeb7

Interventional neuroradiology to treat hyperacute ischaemic stroke

Is effective but good trials are needed to establish exactly who benefits

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Ischaemic stroke causes an enormous amount of morbidity and mortality. In England and Wales about 53 000 people die each year after a stroke, and more than 450 000 people survive with severe disability, at an annual cost of £7bn (€8.4bn; $11bn).[1] Many variables influence clinical outcome, including patient factors—such as the site of vessel occlusion, extent of thrombus, quality of collateral blood flow, and the patient's clinical condition at presentation[2-4]—as well as therapeutic factors, such as the timing and effectiveness of recanalisation of the vessel. Early recanalisation is associated with a fourfold to fivefold increase in the chance of a person being able to function independently and a four to five times reduction in the odds of death.[5] A recent review concluded that interventional neuroradiology techniques are highly effective in achieving vessel recanalisation.[6] Such interventions may come to play a more central role in the management of hyperacute ischaemic stroke.

Currently, the standard treatment for patients presenting up to 4.5 hours after the ischaemic ictus is intravenous tissue plasminogen activator.[7] This treatment is effective in only about half of distal vessel occlusions, but it is relatively low cost.[8] The prognosis for patients with clinically severe strokes secondary to proximal occlusions (most commonly the terminal internal carotid artery and proximal middle cerebral artery) remains poor. More than 10 years ago, a randomised trial showed no benefit for intravenous tissue plasminogen activator in patients with the most severe strokes (those with a baseline National Institute for Health Stroke Scale (NIHSS) score >20), with only one in five with an NIHSS score greater than 10 achieving independent living.[9]

Intravenous tissue plasminogen activator probably has limited ability to break down large vessel occlusions—transcranial Doppler studies have shown that, two hours after treatment, only 44%, 29%, and 10% of distal middle cerebral arteries, proximal middle cerebral arteries, and terminal internal carotid arteries, respectively, achieve complete recanalisation.[8] Recanalisation rates after delivery of thrombolytic agents intra-arterially via a microcatheter directly into the thrombus in proximal middle cerebral occlusions, however, are around 65%.[10] Furthermore, observational studies show that mechanical devices such as stents, thromboaspiration catheters, angioplasty balloons, and other clot retrieval devices improve rates of recanalisation further; reported recanalisation rates with some devices are 80-90%.[6]

Interventional techniques may reduce the need for chemical thrombolytics. Furthermore, such techniques can be used to extract thrombus that is resistant to breakdown by tissue plasminogen activator and achieve recanalisation much faster than traditional chemical thrombolysis. Data from multiple studies and our own experiences have shown that for some patients presenting with severe stroke and proximal vessel occlusion, endovascular recanalisation can achieve excellent clinical outcomes when the anticipated outcome would be poor.[6 11] Prospective studies based on registry data have shown improved outcomes in patients treated with intravenous thrombolysis plus endovascular treatment compared with intravenous thrombolysis alone,[11] and a cost utility analysis suggests that endovascular treatments are cost effective compared with standard medical treatment.[12]

Further evidence from randomised trials is needed to define the full spectrum of patients with stroke who may benefit from such interventions, so that resources may be used effectively.

Any randomised trial that assesses the effectiveness of interventional treatments must consider time since stroke and patient selection. Careful consideration of temporal inclusion criteria and selection of patients for treatment who present beyond the standard therapeutic time window is important. The findings of case series have highlighted a discrepancy between overall clinical outcome and recanalisation rates. Recanalisation rates of 65-90% have been achieved using endovascular techniques but favourable outcome (a modified Rankin score ≤2 at three months) is achieved in only 25-60% of cases.[6] This is probably because some patients are treated too late for recanalisation to be effective. Some studies have included patients up to eight hours after the event.[6]

The RECANALISE prospective cohort study showed the benefit of early canalisation.[11] Ninety three per cent of patients recanalised within 210 minutes were functionally independent at three months, whereas this figure fell to 37% for those recanalised within 260 minutes—"time is brain." The temporal inclusion criteria should therefore be adjusted in future trials, so that only patients with a shorter time window after symptom onset are included. On the basis of current evidence for intravenous thrombolytic treatment, we suggest that arterial access should be achieved by 4.5 hours. This should prevent trials from failing to show any benefit of endovascular treatment because they included too many patients who are beyond rescue.

It is not yet clear how to select cases for endovascular treatment, particularly among patients with less severe stroke or those who present relatively long after the event. Computed tomography or magnetic resonance imaging could be used to assess the volume of established infarct and the site of the arterial occlusion. The site of vessel occlusion often predicts final infarct volume,[2] but depending on the quality of collateral flow, established infarct volume at presentation varies greatly. Patients with good collateral flow will maintain a smaller infarct volume for longer, and it is these patients who may benefit from recanalisation even after 4.5 hours.[3]

Endovascular treatment is provided as standard in some European and American cities, and experience with these techniques is increasing among practitioners in the United Kingdom. Endovascular techniques will probably prove to be the treatment of choice for patients presenting with an ischaemic stroke owing to a large vessel occlusion where early recanalisation can be achieved. However, it will be costly and logistically challenging to provide such services as routine, which is why well designed randomised clinical trials are needed to discover whether managing hyperacute stroke with endovascular recanalisation is effective and cost effective compared with traditional thrombolytic treatment.

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The wide, and often contradictory, range of responsibilities assigned to Monitor sounds more like the brief for a governmental department than for a cohesive "independent" fiscal regulator

The role of regulation in healthcare

Needs further scrutiny before regulatory bodies can perform effectively

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In November 2011, the healthcare think tank the King's Fund published an assessment of the responsibilities and prospects for the newly redesigned Monitor, the independent regulator of NHS foundation trusts.[1] The report explores several sensitive problems that inevitably face a newly beefed up health sector regulator.

Regulation has become an increasingly important part of the political toolbox in European healthcare systems that are funded by taxation. When healthcare providers were directly ruled by a central or regional government office, their decision making discretion was typically limited to informal strategies to create small degrees of autonomy within government directives.[2 3] Regulation was rule based, serving mostly to convey higher level political decisions to lower operating levels of the delivery system.

With the onset of planned markets in the early 1990s, the role of regulation changed. In a provider market where institutions had some degree of competitive freedom, regulation shifted from conveying a fixed content from above to focusing on ensuring that the process of competition down below was fair, that entrepreneurialism and innovation were encouraged, and that the results satisfied political expectations up above.[4] Osborne and Gaebler called the process no less than reinventing government.[5] Political scientists were quick to note, however, that this new type of process focused regulation, particularly when it involved multiple detailed contracts, was much more complex than command and control governing approaches and would require more skill and resources to be successful.[6]

It is no surprise therefore that concerns have been raised about the structure and function of health sector regulators such as Monitor in England. As a recently developed complex area of governmental activity, much can be learnt from "doing." Hence, the common suggestion that the health sector might learn from industrial sectors—utilities in particular, such as water and electricity—that moved earlier into this new type of regulatory arrangement.

Light at the end of the financial tunnel?

The recent King's Fund report raises several questions. How will Monitor balance the financial needs of the payers with the needs, in terms of access and choice, of patients? How will it spot decaying finances in a hospital before services deteriorate and patients might be affected? Conversely, how will it ensure that large hospitals with clever managers don't gobble up their competitors to create new forms of local monopoly? How will it ensure that ostensibly competing providers cooperate to deliver integrated care services for chronically ill elderly patients?

These and similar questions have characterised debates about regulation in several countries, and the King's Fund study provides a useful codification of these ongoing regulatory worries. It also notes recent experiences on these and other problems in other countries (such as the Netherlands), as well as in the available evidence about utility regulation in England.

However, the study does not deal with some key questions that must be answered to chart the broader structural progress of the current regulatory process. Firstly, what is the appropriate balance between state control and market innovation in different subsectors of health systems? Does this balance differ between countries with different political contexts and cultures? What is the regulatory target that Monitor should be expected to hit to ensure that core NHS values are preserved while competitive efficiencies are optimised?

Moreover, the still largely nationalised inpatient health sector in England will continue to be directly accountable to parliament. In light of this, how can regulators create enough space for manoeuvre to become more than just nationalised control of the hospital sector by different means? Indeed, the wide, and often contradictory, range of responsibilities assigned to Monitor sounds more like the brief for a governmental department than for a cohesive "independent" fiscal regulator.

Lastly, it is not clear how this complex set of regulatory responsibilities will play out in what is fast becoming an era of permanent austerity in all welfare service budgets. What happens when—a situation in which most European countries and the United States may soon find themselves—there is no longer any light at the end of the fiscal tunnel.[7] What will happen when there is not enough money?

The King's Fund report raises more questions than it resolves, which is, arguably, what any good study should do. In this regard, it makes a useful contribution to an important health policy debate that is far from over.

Competing interests: None declared.
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