OPEN LETTER TO THE BMA

NHS reform is unnecessary reinvention

The current reforms are an unnecessary reinvention of past NHS structures. Commissioning bodies will be too small for major spending on say dialysis, transplants, and other high cost treatments. For these and for economy of scale (policy development, pharmaceutical advisers, training programmes, etc) commissioning bodies will need to merge—just like primary care groups did on becoming the initial primary care trusts, which in turn were merged into the current 152 organisations. In London, at least, these are now merging again as an interim transitional body to save the millions required not to leave a deficit. Mere polite discussion when the government is about to rip up all existing managing bodies and require GPs to take this on, with no clear promise that they will not be saddled with hundreds of thousands of pounds of individual debt, is just incompetence. The General Practitioners’ Committee was sidestepped by the previous government as the new General Medical Services contract was introduced (remember the promises to continue negotiating over what the core services were, provided we all first voted to agree to the deal or have a worse one imposed on us?).

The BMA is ineffective in negotiating for the benefits of its members and by extension the value democratic accountability should join the growing ranks of health professionals, trade unionists, academics, think tanks, and patient groups that have recognised the weaknesses in the white paper’s detail and content, focusing purely on GP commissioning. However, all of the bodies to be abolished by the proposals (primary care trusts, strategic health authorities, and NHS trusts) are public bodies that meet in public and publish minutes and board papers, whereas the new bodies (consortiums, social enterprises, and foundation trusts) would meet behind closed doors with press and public excluded.

Although primary care trusts (and health authorities before them) are not fully democratic, Lansley’s alternatives are far worse, and could lead to further radical policy changes with no opportunity for public debate. Those who value democratic accountability should join the regional ICDF clinical panel, I watch oncologists struggle with the poor quality clinical evidence on the proposed drugs. Many clinicians understand that we need a rational prioritisation process for NHS drugs and not the ad hoc nature of the ICFD. Attached to the consultation on the proposed fund is an impact assessment. The policy objective is to “recognise the possibility that society may value health benefits provided to patients with cancer more than similar quantities of benefit provided to patients with other conditions.” The use of “possibility” suggests a difficult evidence base. There is some evidence that people value the treatment of severe diseases highly, although the document also acknowledges that the quality adjusted life year (QALY) used by the National Institute for Health and Clinical Excellence (NICE) captures measures of disease severity. It also uses assumptions based on how NICE uses QALY evaluations for cost effectiveness.

The preferred option calculates that the diversion of £200m (€232m; $318m) a year will displace 8000 QALYs (£480m) from patients elsewhere in the NHS. I would be surprised if this opportunity cost did not cause misgivings among the public or elsewhere in the NHS. This level of benefit foregone elsewhere in the NHS needs wider public debate before we become more entangled with the politics around cancer drugs.

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Competing interests: None declared. 1 Peedell C and cosignatories. Open letter to the BMA about the health white paper. BMJ 2011;342:d7. (4 January.)
Cite this as: BMJ 2011;342:d619

INTERIM CANCER DRUGS FUND

Benefits foregone need wider public debate

Anyone involved with the Interim Cancer Drugs Fund (ICDF) will recognise the inconsistencies and contradictions in trying to make it work for drugs with poor clinical effectiveness. As an adviser to the regional ICDF clinical panel, I watch oncologists struggle with the poor quality clinical evidence on the proposed drugs. Many clinicians understand that we need a rational prioritisation process for NHS drugs and not the ad hoc nature of the ICFD.

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Cite this as: BMJ 2011;342:d619

Democratic deficit

The “consultation” on the white paper was a sham from the outset, and it has been no surprise that Andrew Lansley has brushed aside almost every critical response. He has closed his eyes to the evidence that his efforts to break up the NHS and transform it into a market in which taxpayers’ money is used to purchase care from for-profit and non-profit private providers will increase costs, reduce quality of care, and introduce a rampant “postcode lottery” of local inequalities and rationing of care.

Most of the press debate has ignored much of the white paper’s detail and content, focusing purely on GP commissioning. However, all of the bodies to be abolished by the proposals (primary care trusts, strategic health authorities, and NHS trusts) are public bodies that meet in public and publish minutes and board papers, whereas the new bodies (consortiums, social enterprises, and foundation trusts) would meet behind closed doors with press and public excluded.

Although primary care trusts (and health authorities before them) are not fully democratic bodies, Lansley’s alternatives are far worse, and could lead to further radical policy changes with no opportunity for public debate. Those who value democratic accountability should join the growing ranks of health professionals, trade unionists, academics, think tanks, and patient groups that have recognised the weaknesses in the white paper.

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Competing interests: None declared. 1 Peedell C and cosignatories. Open letter to the BMA about the health white paper. BMJ 2011;342:d7. (4 January.)
Cite this as: BMJ 2011;342:d620

What about training?

Of concern is the dearth of discussion relating to education and training. This is a function of all NHS hospitals. There have been great advances in the education of medical and allied health professionals over the previous decades, including training of trainers. Will this be lost?
This political sop is not a fair allocation of NHS resources

The Cancer Drugs Fund white paper makes proposals that go to the core of what is fair allocation of national health resources. The fund is a political sop to the high profile negative press cancer drugs not approved by the National Institute for Health and Clinical Excellence (NICE) have received. But the press is not a good arbiter of how best to make a fair NHS.

The cancer fund is not “extra” funding but money that should be shared across the NHS in the way the NHS was designed to operate—to provide an equal distribution of funding to those in equal need. Cancer patients are no more important than any other group of patients. Welcoming the cancer fund will allow the government to open the door to piecemeal funding in other areas of the NHS.

The cancer fund will pay for drugs that, on the basis of their need-benefit analysis, NICE has decided it is not collectively fair to fund. The very idea of the cancer fund is therefore inequitable and contrary to all that the NHS stands for.

Providing a finite fund that will be administered by consultants in a partisan way will create an inconsistent and unfair model of resource allocation. The cancer fund represents a diversion from the fair allocation of NHS resources for maximum societal benefit and should not be supported.

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Competing interests: None declared.

1 ST is a lay member of the Royal College of Radiology’s clinical oncology liaison group (although these views are her own and do not represent those of the RCR).

PARACETAMOL

A narrow therapeutic ratio? Really?

It is discouraging that the BMJ published a “lesson of the week” warning us of “chronic toxicity” from paracetamol (N-acetyl-p-aminophenol; APAP) without a counter argument. Although paracetamol can be life threatening after intentional overdose, when taken in anything less than extremely large doses it is one of the safest drugs ever created. Fear mongering about paracetamol will surely lead to the substitution of far more dangerous alternatives.

Before N-acetylcysteine became available, acute liver failure occurred in about 3% of those who took an overdose of 150 mg/kg (although most of that small group ended up with no chronic liver failure); is there any other drug that is so rarely toxic at 10 times the standard therapeutic dose? Just how is this a narrow therapeutic ratio?

The authors present two cases of liver failure associated with repeated use of paracetamol but fail to see what these cases imply. Firstly, they don’t question that liver failure was caused by paracetamol, even though one patient was an alcoholic and the other was an adult male weighing only 30 kg. Secondly, case reports by definition highlight unusual outcomes. They can provide useful lessons, but case reports describing rare events in the setting of an extremely common condition (millions of people use paracetamol) show how unlikely such outcomes are.

A far larger series identified 47 cases with a purported (extremely tenuous) relation to chronic paracetamol use by scouring the literature and all reports to the Food and Drug Administration, plus their own referral centre’s experience over 20 years. Compare this to thousands of cases of fatal gastrointestinal haemorrhage, each year, from non-steroidal anti-inflammatory drugs (a class of drugs far less toxic than most drugs in use). Even if all 47 cases (and every one ever published) were caused by paracetamol (which defies credibility), it would be eloquent testimony to the drug’s safety.

The authors predict that we will see legions more such cases in the future, given continued widespread paracetamol use. Why haven’t we already seen this epidemic, after many years of widespread use?

The only real problem with paracetamol—a drug used safely by scores of millions of people, that at most causes almost no harm (unless taken as a large overdose)—is that it is far too inexpensive to qualify as a great drug.

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Competing interests: None declared.

1 Claridge LC, Ekstee B, Smith A, Shah T, Holt AP. Acute liver failure after administration of paracetamol at the maximum recommended daily dose in adults. BMJ 2010;341: c7389. (30 December.)

Cite this as: BMJ 2011;342:d621

Author’s reply

Hoffman questions the cause of liver failure in the cases we described.1 Patient 1 weighed 30 kg because of chronic malnutrition secondary to Crohn’s disease, which increased his susceptibility to paracetamol induced hepatotoxicity. The second patient’s rapid onset of liver failure, with serum aspartate aminotransferase peaking at over 7000 U/L and subsequently falling quickly, is not consistent with alcoholic liver injury. Moreover, both patients received paracetamol under direct supervision.

We acknowledge that these cases are rare, but all reported cases have recognisable risk factors, indicating preventability.

If we consider cumulative daily doses of paracetamol rather than single one off doses, the therapeutic index certainly becomes narrower; many cases of liver injury occur after unintentional overdoses of as little as 5-7.5 g/ day (www.fda.gov). In the US this has prompted the Food and Drug Administration to propose decreasing the maximum daily dose from 4 g to 3.25 g.2 Our patients repeatedly received higher than therapeutic doses for their weight, and children of equal weight receive significantly lower doses as a matter of course.3

Another fatal case of liver failure secondary to maximum dose paracetamol in an underweight adult was recently reported by the UK press. Two deaths in the UK in less than 12 months is hardly a “negligible rate of harm.”

I agree that paracetamol at recommended doses is safer than other analgesics, but it can be harmful to some, and we should not ignore recognisable risk factors.

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Competing interests: None declared.

1 Hoffman JR. And just how do you define narrow therapeutic ratio? BMJ 2011;342:d625.


3 Wilne SH. Rapid response. Importance of patient weight. www.bmj.com/content/341/bmj.c6764.full/reply#adm_el_246265.


Cite this as: BMJ 2011;342:d628

INFECTIVE ENDOCARDITIS

NICE originally called for register

We agree with Stern and other correspondents that the incidence of infective endocarditis urgently needs to be monitored.1 The publication of our clinical guideline on prophylaxis against infective endocarditis caused controversy in recommending that antibiotic prophylaxis to prevent infective endocarditis should not be
given to adults and children with structural cardiac defects at risk of infective endocarditis undergoing dental and non-dental interventional procedures. We know of at least one primary care trust that has decided not to implement the guideline fully. Since then, the National Institute for Health and Clinical Excellence (NICE) has received letters reporting anecdotes of individual patients developing infective endocarditis after a dental procedure in the absence of antibiotic prophylaxis. These are of course all personal tragedies, but unfortunately they provide no further evidence to inform the debate about the role of antibiotic prophylaxis or any future guidance.

The guideline recommended that because infective endocarditis is a rare condition “research in this area in the UK would be facilitated by the availability of a national register of cases … that could offer data into the ‘case’ arm of proposed case-control studies.” We have encouraged cardiologists who have contacted us to take up this recommendation of a national register of cases but are not aware of any attempt to do this.

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Competing interests: TS, FM, and PL are employees of NICE. TS led the NICE short clinical guidelines team that developed the prophylaxis against infective endocarditis guideline.
1 Stern SR. Time to monitor incidence after NICE guidance. BMJ 2011;342:d2121. (11 January.)

Cite this as: BMJ 2011;342:d633

FLU QUESTIONS AND ANSWERS

Flu’s impact on intensive care
O’Dowd’s report on the response to the winter flu surge does not mention the large impact the surge has had on intensive care units (ICUs),1 which responded to the crisis by rapidly increasing capacity through staff working additional hours and by adapting operating theatres and postoperative recovery units. Capacity for extra corporeal membrane oxygenation (ECMO) for the most severely affected cases was increased from 5 to 25 beds.2 Across the UK more than 1000 critically ill adult patients with flu were admitted during the epidemic, and 50 have died.

This should be seen in the setting of overall provision of intensive care in England. In 2010 a total of 3622 general and specialist adult ICU beds were available for general and emergency care, the remainder being allocated to cardiothoracic surgery and other specialist services. A recent international comparison shows that the UK’s 3.5 ICU beds per 100 000 population is by far the lowest of seven developed economies in Europe, and around 15% and 25% of the proportion in the United States and Canada respectively.3 Not surprisingly, 65% of UK intensive care specialists reported that admission to intensive care was commonly limited by bed availability.4

Despite severely limited resources and massively increased demand, the intensive care community has sustained a clinically excellent service—as shown by the comparatively low mortality5—but at the expense of other clinical services dependent on this low provision of ICU beds. Adequate resourcing of intensive care remains a critical issue for the NHS.6

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Competing interests: None declared.
1 O’Dowd A. Influenza: questions and answers. BMJ 2011;342:d190. (12 January.)

Cite this as: BMJ 2011;342:d640

RESEARCH APPROVAL

The regulation killing health research in the UK
At last, the fight back against the “complex and bureaucratic regulatory environment” of health research in the UK has begun.1 2 However, although the recommendations of the Academy of Medical Sciences are laudable, the report ignores an important aspect of the regulatory process that is a major disincentive to many NHS clinicians.3

The initial step in clinical research is to apply for ethical and research and development approval by completing three forms electronically through the Integrated Research Application System (IRAS).1 This entails filling in a questionnaire whose latest dataset is 27 pages long, consisting of four parts and 109 items. A 21 item checklist also has to be completed, and a long list of supporting documents provided. Simple? Definitely not. The IRAS forms have been updated eight times in the past two years.

The IRAS On Line Form User Manual is 22 pages long. The e-Learning Training Module on the IRAS website takes one hour to complete.

This complex application process may not trouble a large drug company or academic department, but it is an issue for busy clinicians. The same time consuming forms have to be completed irrespective of potential risk, the application process being little different for a questionnaire based study and a randomised trial of a new drug, for example. In contrast, ethical approval is not required in the United States for research associated with no risk. We also doubt that the European Clinical Trials Directive, which forms the basis of many of the regulatory processes in the UK, is so literally enforced elsewhere in Europe.

We need proportionality in respect of the data required by IRAS. Without it, the current wane in research by clinicians working in the NHS will continue. And we should not underestimate the contribution made to medical science by those working on the shop floor.

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Competing interests: None declared.
2 Dillner L. UK needs new health research agency to speed up approval process. BMJ 2011;342:d185. (11 January.)

Cite this as: BMJ 2011;342:d642

REDUCED ACCESS TO DATABASE

Publicly available databases accelerate academic production
Electronic health databases are popular as research materials in medical studies.1 Our analysis of publications that used the general practice research database (GPRD) as their main data source found that from 1995 to 2009, GPRD had attracted 1251 authors from 22 countries. In total, 749 studies were published in 193 journals, covering 58 study fields—from pharmacology and pharmacy (26.4%), general and internal medicine, to economics. The number of GPRD studies is increasing rapidly and is expected to double by 2015.

Taiwan’s national health insurance research database (NHIRD), composed of de-identified medical claims from 99% of Taiwan’s 23 million people, is available to any researcher in Taiwan.2 A small data processing fee is charged—TW$500 ($11; €12.6; £7)—per compact disc or TW$200 per gigabyte of data. Like GPRD, NHIRD also has
great academic influence. In a 10 year analysis, we found 383 NHIRD studies conducted by 667 authors, published in 210 journals, covering 60 study fields—from healthcare sciences (14.4%), to economics, and computer science. Not only clinical but also general health disciplines benefited from NHIRD. The number of articles doubled every two years—a growth rate two times greater than that for GPRD studies.

These analyses suggest that public health databases promote scientific research, and even more so when the barriers for use are low. To promote healthcare, data holders at a national level should consider minimising financial and technical constraints on the reuse of data for research purposes.

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Competing interests: None declared.

1. Knietowicz Z. End of free access to database will shrink UK generated research, says expert. BMJ 2011;342:c7455. (10 January.)

2. National Health Research Institutes. Introduction to the national health insurance research database (NHIRD), Taiwan. 2011.


Cite this as: BMJ 2011;342:d637

ACCESS TO CLINICAL TRIAL DATA

Data monitoring committees and selective outcome reporting

Selective outcome reporting leading to biased treatment and adverse effect estimates could be discerned by independent re-evaluation of full outcome data that are made publicly available after publication of a clinical trial. However, it would be more efficient to use data monitoring committees to do this while the trial is being conducted. With their in depth understanding of the study objectives and protocol, as well as access to fully disclosed results as they accumulate, these committees are well placed to gauge compliance with the collection and use of data for all prespecified outcomes from the start of a trial to its completion. Data monitoring committees are independent and widely perceived to be extremely competent. Using these committees to review and approve the completeness of outcomes reported before publication would enhance the credibility of all studies and make them less likely to be biased. The DAMOCLES Study Group recommends that data monitoring committees “ensure that trial results are published in an unbiased, correct and timely manner” and that the committee discusses final data and their interpretation with study investigators. The ability to monitor for selective data collection and use while the study is being conducted improves the validity and credibility of submitted manuscripts, eliminates the need for resource intensive post-publication re-evaluation, and averts disseminating biased estimates to journal audiences in the first place.

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Competing interests: None declared.


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OUT OF HOSPITAL CARDIAC ARREST

Time for a national register

Knietowicz highlights the disparity in survival from cancer between the United Kingdom and other countries. Cancer survival is closely studied, with large investment from government bodies and charities to ensure accurate determination of incidence and survival to drive improvement. Cancer is responsible for around a quarter of deaths in Europeans aged 45-65.

Out of hospital cardiac arrest is common, occurring in around 66 per 100 000 Europeans every year, with cardiovascular disease accounting for 41% of all European deaths. The exact incidence of out of hospital cardiac arrest is unknown because few countries collect and report data accurately, despite the availability of the Utstein template, an internationally agreed data set. The analysis by Moon and colleagues contains a flawed assumption in analysis.

Survival from out of hospital cardiac arrest remains poor, with rates varying from 1% to 20% and disparity between and within countries. Unlike cancer, survival from out of hospital cardiac arrest depends on only four key elements, the chain of survival: early recognition and summoning of help, early cardiopulmonary resuscitation, early defibrillation, and advanced post-resuscitation care. Each element can be improved locally to dramatically improve survival.

Establishing national registries for out of hospital cardiac arrests, reporting survival data, and improving the local links in the chain of survival would result in many more lives being saved.

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Competing interests: None declared.

1. Knietowicz Z. Cancer survival in the UK and Denmark lags behind Australia. BMJ 2010;341:c7372. (22 December.)

2. European Public Health Alliance. What are the leading causes of death in the EU? www.epha.org/a/r2352.


Cite this as: BMJ 2011;342:d478

NHS DRUG BUDGET

Flawed assumption in analysis

The analysis by Moon and colleagues contains a flawed assumption: that citalopram is a generic variant of escitalopram. In reality, citalopram is a racemic mixture and escitalopram the active S-enantiomer. For nearly a decade the presence of the R-enantiomer in citalopram has been known to impair the function of the S-enantiomer, effectively reducing its potency and efficacy. This explains the body of evidence showing that escitalopram is more efficacious and better tolerated than citalopram, even when citalopram is given in doses delivering equal amounts of the S-enantiomer.

As this is but one of several examples in psychiatry where pure enantiomers show different pharmacology from racemic mixtures, generic racemic drugs cannot be assumed to equate to pure enantiomers. For this reason the European Medicines Agency is currently reviewing the regulatory position on enantiomers.

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