

# reviews

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## Editor in the eye of a storm

Is the editor of a medical journal responsible for the way its contents are reported, and the quality of the ensuing debate, as well as the accuracy of the material itself? It is a question that Dr Richard Horton, editor of the *Lancet*, and one of the figures in the eye of this week's media storm over the MMR (measles, mumps, and rubella) vaccine, has answered unequivocally in the past.

In an essay entitled "Vaccine Myths"—included in his book *Doctors, Diseases and Decisions in Modern Medicine*, which was published last year (reviewed *BMJ* 2003;327:399)—Dr Horton recounted the events that followed the *Lancet*'s publication of Dr Andrew Wakefield's 1998 study that sparked the suggestion of a link between MMR and autism. He says: "Although I knew this paper would be controversial, I did not expect the level of vituperative attack and personal rebuke that followed. I was terribly and, looking back now, embarrassingly naive. I should have met with the Royal Free team before they held their press conference. I should have at least tried to persuade Andrew Wakefield not to recommend splitting the vaccine. [It was at the press conference that Wakefield said that parents should be given the choice of single vaccines, rather than just the MMR.]

"All in all, my attitude was far too laissez faire. If this is what critics meant—and still mean—by reckless, then I am guilty of that charge. I failed to do enough to manage the media reaction to this work. Until the Wakefield paper, I had not seen this media management role as one for a scientific medical journal editor. I now see it as one of my main responsibilities."

Observers must wonder how that opinion has fared in the light of this week's events.

Last Friday BBC Online quoted Dr Horton saying that with hindsight the *Lancet* would not have published the paper. "There were fatal conflicts of interest in this paper. In my view, if we had known the conflict of interest Dr Wakefield had in this work I think that we would have strongly affected the peer reviewers about the credibility of this work and in my judgment it would have been rejected."

## Revealed: MMR research scandal

ST investigation exposes scientist's 'fatal' conflict of interest

Full details are disclosed in the three-month investigation that has uncovered a medical scandal at the heart of the world's vaccine wars over MMR.

Andrew Wakefield, the doctor who challenged the alleged link between measles, mumps and rubella vaccine and autism by using children, must disclose his conflicts of interest to his colleagues on The *Lancet*, the professional journal that published his findings.

The investigation has found that when he received payment to avoid MMR, and published research claiming a link with autism, he did not disclose his research funding through Visceral, the *Lancet*'s fund-raising charity. The funding, Francis said, also meant that the finding

was not independently verified, but he said he was not contacted with the investigation findings that he was engaged on. He denied involving his colleagues on The *Lancet*.

The scandal arose from the journal's publication in February 1998 of a scientific report on the "linking" in the case of 12 autistic children, apparently administered routinely to the Royal Free hospital in north London in 1998-97.

Wakefield was the lead author of the report. He wrote that the parents of eight of the 12 children blamed MMR; they said symptoms of autism had set in within days of vaccination.

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The *Sunday Times* article that sparked the latest MMR controversy

He also said: "As the father of a three year old who has had the MMR, I regret hugely the adverse impact this paper has had." But he added: "Professionally, I don't regret it. The *Lancet* must raise new ideas."

These statements followed a meeting at the London office of the public relations company Bell Pottinger on Wednesday, attended by the firm's executive Abel Hadden, Dr Wakefield, and three members of *Sunday Times* staff. The meeting was apparently to discuss material uncovered by Brian Deer, a freelance investigative journalist, working for the *Sunday Times*. Abel Hadden told the *BMJ* that he had arranged the meeting at which he was representing Visceral, a medical research charity for intestinal diseases, established in 2000, of which Andrew Wakefield is chief medical scientist.

### "Professionally, I don't regret it"—Richard Horton

The allegations raised by Brian Deer's investigation—published in last weekend's *Sunday Times* and widely followed up in print and broadcast media—concerned the ethics of Wakefield's research study and claimed a failure to disclose a conflict of interest. It revealed that Wakefield was paid £55 000 (\$102 690; €81 817) by the Legal Aid Board to investigate children who were allegedly vaccine-damaged for a possible legal action by their parents. A press statement from the *Lancet*, issued the Thursday before Deer's article was published and making no mention of the *Sunday Times*, expressed "regret" that this funding was not disclosed. The *Lancet* said it would "pursue a course of full disclosure and transparency" and publish a response to all the allegations.

In addition to the two page investigation by Brian Deer, the *Sunday Times* also carried

an opinion piece by Dr Evan Harris, Liberal Democrat member of the Commons science and technology committee calling for an independent inquiry into the way the research was carried out. Dr Harris, a member of the BMA's ethics committee, said something similar to the Kennedy inquiry into the deaths of babies at Bristol Royal Infirmary was required.

The controversy over MMR has been one that has played out in the media all along; in the past week it has almost come to a head. However, instead of breaking down battle lines between some sections of the media and the Wakefield camp on the one hand, and the medical and scientific community and the government on the other, positions seem only to have become further entrenched. That most staunch defender of Dr Wakefield, the *Daily Mail*, claimed on Monday that he had been the victim of a smear campaign. By Tuesday the paper suggested that parents had been betrayed by the whole affair. Instead of Andrew Wakefield himself in the media firing line, it is the *Lancet* that has found itself under scrutiny. Perhaps it was in a bid to forestall this that the *Lancet* went public over the whole affair last week in advance of the *Sunday Times* story, thus angering Brian Deer.

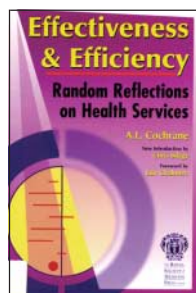
On Tuesday Dr Horton told the *BMJ* that the UK needed an independent body to investigate the conduct of research. But he added that authors had a duty to reveal the context of their work and potential conflicts of interest. "The whole system depends on trust and honour," he said.

And the duty of medical editors? "To report new thinking and make sure that the context is reasonable."

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## Effectiveness and Efficiency: Random Reflections on Health Services

A L Cochrane



Royal Society of Medicine Press, £12, pp 120  
1 85315 394 X  
www.rsmppress.co.uk/  
bkcochra.htm

Rating: ★★★★★

Archie Cochrane was an epidemiologist with a maverick streak. In 1935, as a lone medical student, he marched through London carrying a home made placard that read, "All effective treatments must be free." According to him, nobody noticed. In this seminal book, first published in 1972 by the Nuffield Provincial Hospitals Trust and issued in this imprint in 1999, he called for an international register of randomised controlled trials, and for explicit quality criteria for appraising published research, but neither goal was achieved in his lifetime. Today, the Cochrane Controlled Trials Register has more than 400 000 entries, and an international movement to improve the methodology of research synthesis also bears his name ([www.cochrane.org/index0.htm](http://www.cochrane.org/index0.htm)).

A passionate early advocate of the NHS, Cochrane described it in *Effectiveness and Efficiency* as "a favourite child who is now showing signs of delinquency." Making treatments free had created two perverse incentives: patients expected a treatment for every complaint, and doctors felt compelled to provide one. Cochrane's wartime experience as the sole medical officer for 20 000 inmates in a German prisoner of war camp—in which only four people died, three of whom were shot by their guards—convinced him that the vast majority of illness was self limiting and that medical treatments were generally incidental to recovery. He made it his mission to save the public (and the taxpayer) from the perils of ineffective interventions.

One of the most perceptive sections of the book is Cochrane's review of the Universities Group Diabetes Program study—a well designed, multi-centre randomised trial of the effects of sulphonylureas on the outcome of type 2 diabetes, which showed no benefit (and, indeed, net harm) from this class of drug. This controversial finding, newly published when Cochrane was writing, was largely ignored by diabetologists, perhaps because clinicians are less receptive to negative studies than they are to positive ones. Subsequent trials have, arguably, failed to refute the UGDP findings, but sulphonylureas remain widely prescribed. Cochrane lamented that the well-meaning prescription of ineffective medication had spawned a

mushrooming industry of hospital outpatient services, whose knock-on effects included "... the increased size of outpatient buildings and the increased staff required to run them; the increased ambulance services for the patients; the increased parking space around hospitals; the increased travelling for elderly ill patients; and the increased loss of time from work by otherwise fit patients."

Effectiveness (whether treatments work—a dimension we now call efficacy) and efficiency (optimal use of resources) were, Cochrane said, two fundamental pillars on which the NHS ought to be run. He added a third—equality of provision across socio-economic groups (which we now call equity), and called for better data, better training, more systematic reflection on practice, greater use of computers, and the setting up of independent watchdogs to monitor standards in the NHS. As Cochrane recognised in the book, efficacy, efficiency, and equity are not exhaustive dimensions of quality. Along with acceptability, access, and relevance, they became the "Maxwell Six" (*Quality in Health Care* 1992;1:177-9), which inspired the first attempt at a national performance framework for the NHS, published on the delinquent child's 50th birthday, and to which the contemporary quality connoisseur would now add risk management, cultural congruence, partnership, and probably several more besides.

Cochrane was pilloried by colleagues for appearing on television to promote abortion and to claim (rightly, at the time) that there was no evidence of benefit from routine cervical smears. He thumbed his nose at "expert opinion" and denounced the Medical Research Council for its snobbery towards applied and occupational research ("the MRC investigated God-made diseases while others could investigate man-made diseases"). He delighted in the results of a randomised trial, published in the wake of a high profile American campaign to build a state-of-the-art coronary care unit in every hospital, which showed that heart attack patients might just as well stay at home (*BMJ* 1972;3:334-7).

Cochrane's raw moral courage, his indefatigable pursuit of the truth, and his irreverence towards the scientific establishment remain an inspiration to those of us whose research time is increasingly spent in petty correspondence with ethical committees, grant giving bodies, and journal editors. His predictions about the lack of efficacy of treatments (for example, his hypothesis that thrombolysis would not influence outcome in myocardial infarction) were wrong as often as they were right. But he taught us to question practice systematically, and as such prepared the ground for both applied research and quality improvement in the NHS.

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The *BMJ* is interested in publishing rereadings of other classic medical books. If you have any suggestions for titles that we might include, email [tjackson@bmj.com](mailto:tjackson@bmj.com)

### NETLINES

- Visit the US-based <http://bms.brown.edu/pedisurg/Brown/IBCcategories.html> for a nice collection of paediatric surgical images. There are more than 150 clinical pictures available, covering subjects from abdominal wall defects to trauma. Pointing on an image reveals its caption and clicking on a picture enlarges it. The images can be downloaded as long as it is for individual use and not for profit, although their source should be acknowledged. For specialists and non specialists alike there is some great educational material here, as well as links to other useful sites.

- There is often much good and relevant information to be found on many of the websites run by national ministries of health. The problem is usually finding it. Deep within the website of the New Zealand Ministry of Health is a valuable list of newsletters ([www.moh.govt.nz/publications/newsletters/](http://www.moh.govt.nz/publications/newsletters/)). While some of these have distinct local appeal, such as Maori Health Directorate News, others have much wider relevance, such as the newsletters concerning health e-news, AIDS New Zealand, and public health perspectives. Each section contains an archive that could prove interesting to many readers.

- Best evidence topics or BETs were developed at Manchester Royal Infirmary's emergency department to provide rapid evidence based answers to clinical questions ([www.bestbets.org](http://www.bestbets.org)). The topics mainly focus on emergency medicine, although the database is expanding to include other specialties, such as cardiothoracics, nursing, primary care, and paediatrics. Visitors can search by title, topic, or keyword. It is also possible to download checklists as PDFs to help in appraising medical literature ([www.bestbets.org/cgi-bin/public\\_pdf.pl](http://www.bestbets.org/cgi-bin/public_pdf.pl)).

- The Bradford general practice vocational training scheme has brought together a wide range of educational resources ([www.bradfordvts.co.uk/Online%20Resources.htm](http://www.bradfordvts.co.uk/Online%20Resources.htm)) that will be useful to GP registrars. These include documents, tutorials, and PowerPoint presentations on non-clinical subjects such as audit and information technology, and clinical topics such as dermatology, psychiatry, and palliative care. There are also sections for trainers and senior house officers.

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We welcome suggestions for websites to be included in future Netlines. Readers should contact Harry Brown at the above email address.



## Battle Hospital: Medics at War

Channel 4, 27 February at 7 30 pm

Rating: ★★

As the conventional phase of the recent Iraq war ended, the padre conducting a service for the personnel of 202 Field Hospital said, "We have stood up against tyranny and won." The rest of this documentary on the work of the hospital would have given most viewers a different impression. Nearly all admissions were Iraqi civilian victims of trauma, many of them children. Cue close-up after grisly close-up of surgical debridement, skin grafting, unstable fractures, punctured bowel. Modern war inevitably generates such scenes, and television lets us all share the resulting sense of horror and futility.

*Battle Hospital* followed the 650 men and women of 202 Field Hospital, just across the border from Iraq, through the war and just afterwards. Although thankfully few of the 200 beds and seven operating theatres were

needed for British soldiers, there was plenty of scope to film civilians injured directly or indirectly through the conflict, and the programme makers seem to have missed no opportunity. Later, when the conventional war was over and the Iraqis repatriated, more reflective footage showed staff questioning the war, the reasons for being there, and the need to stay. The programme ended in a distinctly minor key.

At about the time that the field hospital staff were wondering whether war could be justified and why they were there, I was beginning a stint as public health adviser to the Coalition Provisional Authority in Baghdad. It was clear that the Iraqi population faced major immediate public health threats, not the result of the war, but partly the result of the systematic running down of public services by Saddam during the 1990s. Remaining services then suffered badly from the lawlessness after the war. Coalition personnel, many of them military, threw themselves wholeheartedly into countering these problems. Just how much the security problems hampered us from the start is now more widely realised.

My own experience was that almost all Iraqis welcomed the removal of a repressive regime, and wanted a properly constituted Iraqi government. A few, however, wish to prevent reconstruction, regardless of consequential damage to the innocent. They have

plenty of cash to bribe poor and unemployed people to shoot from behind crowds, throw grenades at guard posts, and fire rocket-propelled grenades at vehicles and buildings.

Watching *Battle Hospital* I remembered all this, and more, very clearly. I remembered the team from a US civil affairs battalion that most often provided my transport and escort. Their professionalism was impressive, their comradeship and good humour unflinching, their sense of purpose in righting wrongs unflagging. Two weeks after I left Iraq, the US newspapers reported an attack on that team. Three of the soldiers that I knew as comrades were seriously wounded by shrapnel and gunfire. Another is dead. Our Iraqi interpreter was also killed. They were going to check a water treatment plant.

Can war be justified? How do you trade off the wounding and death of soldiers, civilians, and children against the ravages of mass murder, starvation, and deliberate deprivation? I don't know, but I'm with the padre on this: a cruel despot has been overthrown, and the world is better in consequence. I think my friends—and 202 Field Hospital—deserve to be remembered for that.

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A longer version of this article is available on [bmj.com](http://bmj.com)



## How PR firms use research to sell products

In the past month we have seen some pretty astonishing research. Studies have proved that moving to the countryside, drinking wine, or discussing your relationship problems in bed can improve sexual problems. Owning a pet helps you recover more quickly from illness, testosterone causes unsafe sex, and if your eyes are brown or green they are officially the "wrong" colour. But texting is good for your mental health.

You may not have been privy to these discoveries unless, like us, you have an interest in what research appears in the lay media, or are regularly targeted by public relations companies.

While many questions have been asked about research undertaken by pharmaceutical companies, until now there has been a tendency to ignore the activities of PR companies, which have begun using "research" to sell products. They conduct a "study"—usually a "survey"—and aggressively target the press, making sure the coverage names their product. The result is quick and dirty research, with cheap advertising.

It is easy to dismiss such work, but, given that health is a favourite topic for the PR study, we ought to be concerned—particularly because PR companies have big budgets to promote their research, to the exclusion of more reliable, ethical work. Although the Royal Society is currently looking at how scientific research is reviewed and reported, it seems that PR studies may be slipping through the net.

PR research is intrinsically flawed because it is completed in a short space of time with no ethical approval nor peer review. Often the PR company has decided on the outcome way before the study begins. Where experts are involved they are unlikely to design or analyse the research, and are often provided with quotes to say about the study by the PR company. Whereas research undertaken with NHS staff or patients must now comply with the research governance framework, PR companies have no such responsibilities when contacting members of the public outside of the NHS. For example, one company wanting to promote a new treatment for thrush asked one of us (Petra Boynton) to endorse a high street survey that asked passers-by if they had a sexually transmitted infection, including HIV (she declined). Such a study would not be possible in an NHS research environment.

Such studies are driven by potential headlines, not a hypothesis or an awareness of existing data. So PR research has outcomes that directly contradict existing evidence, make no reference to it, or

replicate it on a far shoddier level (for example a magazine survey of the nation's health may hit the headlines, even though national health data also exists).

Because PR survey results are presented as startling, journalists may see a good headline, a light story, or a way of meeting a looming deadline. We estimate that the average magazine or newspaper journalist will be targeted by several PR companies a day. Since PR studies frequently use big numbers—the magic 1000 participants—some journalists are also beginning to distrust research that has smaller samples, perhaps meaning that many health studies, particularly qualitative ones, are ignored.

There is a danger that media outlets could become wall-to-wall PR. This is going to be an increasingly important issue for all of us involved in high-quality, ethical health research. Now it is time to extend the debate before the public becomes completely disillusioned with so-called research.

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**Will Callaghan** health journalist, London

Competing interest: PB has completed PR funded research in the past.

## PERSONAL VIEW

## An unfinished trip through uncertainties

In mid-1997 I went for blood and other tests after an episode of back pain. A monoclonal electrophoretic peak and a spinal lesion of uncertain origin were found. After a few months of further tests I was given a diagnosis of monoclonal gammopathy of uncertain significance (MGUS). I was no longer a subjectively healthy man but a potentially ill person, with considerable anxiety. MGUS is one of those strange nosological entities of modern medicine—which is so good at creating “new diseases” without necessarily knowing how to cure them. The medical literature didn’t help much. Several small studies reported a cumulative risk of malignant transformation of MGUSs of between 7% and 19%, with the likeliest estimate of annual risk of transformation around 1%, but without clear predictors.

I was prescribed blood tests every six months to monitor any such transformation. The years went by, during which my levels of anxiety varied, increasing at times of testing and whenever any personal or work decisions loomed. Was it worth monitoring MGUS while I was symptomless? What should be done with the slowly increasing monoclonal peak? It was not a good sign, but there was still nothing to be certain about.

An ironic sense of déjà vu helped me, particularly when I was fed up with testing. I had spent several years of my professional life fighting the excesses of medicalisation in oncology, particularly unduly intensive surveillance (follow up) among potentially ill but asymptomatic people. What did we know about treating myeloma at an early stage? Not much: just three small trials, published between 1993 and 2000, failed to identify any benefit in early over deferred treatment. So, too little evidence for a fully informed decision, but enough to decide to wait—in consultation with my doctors—before opting for more aggressive treatment.

Time passed, and in 2001 another step in my “transition” was made. I no longer had MGUS but smouldering myeloma. Still, the consensus was for no active treatment. In December 2002, less than five years after MGUS appeared, I became a multiple myeloma patient. The time for thinking about treatment had come. Haematologists agree that important progress is now being made in treating multiple myeloma. The literature now documents better results for high dose chemotherapy and autologous haematopoietic stem cell transplantation than for the traditional treatments, with improvements in event free and overall survival.

I completed my first treatments with high dose chemotherapy and autologous haematopoietic stem cell transplantation in April

2003. The result: complete remission with bearable toxicity. Then came the time for the latest (so far!) decision. Could a second transplant improve results? The evidence amounted to four randomised controlled trials, whose results haven’t yet been fully published (though the results of at least one had been presented at several specialists’ meetings); a few observational studies; and the direct clinical experience of my doctors (who favoured the second transplant option). I eventually opted for the second transplant. I’m now busy driving up my and my fellow patients’ survival curves.

What are the lessons? Firstly, that as a patient I felt even more strongly about what

### Could a second transplant improve results?

I’ve been fighting for throughout my career. Research results should be easily accessible to people who need to make decisions about their own health. The delay in the combined analysis of the four

randomised controlled trials struck me as a case in point. Why was I forced to make my decision knowing that information was somewhere but not available? Was the delay because the results were less exciting than expected? Or because in the evolving field of myeloma research there are now new exciting hypotheses (or drugs) to look at? How far can we tolerate the butterfly behaviour of researchers, moving on to the next flower well before the previous one has been fully exploited? Unfortunately this is possible in a world where clinical research has become dominated by commercial interests. When you are a patient you wonder how (we) researchers can keep forgetting the principle that the priority should be collaboration for better hypotheses, not competition.

Secondly, my desire to participate in decisions was stronger than ever. As a special patient cared for by excellent doctors I was enabled to make informed choices. But I’ll never forget my anguish when the central venous catheter was positioned, not knowing why it was being placed or for how long. It’s also hard to forget the time I spent wondering how long it would be before my red hair came back and how often I would lose it in successive treatment stages. All these things had been mentioned, but not with the attention they should have been, even when the technical aspects of care were excellent.

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My special thanks go to Mariangela, Elisa, and Valeria, whose support never made me feel lonely; Tiziano Barbui, Alessandro Rambaldi, and the nursing team at the Bergamo haematology department for their frank, competent, and touching help; and all my friends and colleagues for their incredible—and at times unexpected—warmth and closeness.

## SOUNDINGS

## Weapons of mass destruction

The agricultural revolution was the first quantum leap in manipulating the environment and the industrial revolution was the second. The medical revolution is the third. Domestication, the harnessing of stored energy, and the eradication of hostile species were necessary before man could invade all niches on earth and multiply. The securement of man’s biosphere began with the battle against lion and bear and wolf. Now the biological enemies are microscopic and submicroscopic—and our heroes are Jenner and Pasteur and Fleming rather than Theseus, who slayed the Minotaur, Perseus, the killer of Medusa, or Hercules, the accomplished exterminator of dangerous megafauna.

Our biological, chemical, and physical warfare against multitudes of living things is not only directed against those species that invade humans, but also against their vectors, pathogens to our domestic animals and plants, the vectors of these pathogens, and all living things which compete with us and our stock or cultivars.

A completely germ free world is unattainable, but is it a desirable objective? It entails environmental changes that represent new dangers to man and his chattels. Take antibiotic warfare, for example. Microbes are more resilient than we thought; 50 years of broadcasting poisonous substances has had little impact on the pyramid of life.

A justification for a campaign against infection may sound unnecessary. Of course, we do not want tuberculosis, not even in our cows, and we do not want rabies—even if this means doing away with the bat. The combined use of insecticides, pesticides, and herbicides can make economic sense, but only if economy is interpreted as maximising returns over a given period.

If species diversity is desirable, does the concept afford protection to the mosquito and even pathogens or only to the African violet, the Californian condor, and the panda?

The discovery that fanatical hygiene, antibiotic use in infants, and perhaps even vaccinations are detrimental to the maturing immune system and are associated with allergies, asthma, and autoimmune disease should be a warning: our aggression against the rest of the universe is demonstrably detrimental to our wellbeing.

**Imre Loeffler** *editor, Nairobi Hospital Proceedings, Kenya*