Saturday 31 July 2004

BMJ

Clinical research under the cosh again

This time it is ethics committees

Education and debate
pp 277-89

Today the *BMJ* publishes a clutch of papers on the regulation of clinical research by ethics committees.[1–5] All describe, in one way or another, how ethics committee review may impede and delay research, sometimes even to distort the methods so much that the conclusions are flawed and patients damaged—an unintended unethical consequence.

Although this is not just a problem in the United Kingdom, to know exactly what is going on in other countries is difficult. If the situation is anything like that in the United Kingdom it will be confusing, changing all the time (just last month the UK government notably altered its human tissue bill), and made even more confusing by varying guidance from official bodies such as the General Medical Council and the BMA. Clearly, international differences are a particular problem for multicentre research across national boundaries. For example, unlike in the United Kingdom, the United States has provision for waiver of consent for research including patients with sudden mental incapacity, such as those with cardiac arrest.[6]

But even within the United Kingdom there is confusing variation. In Scotland, but not quite yet in England, legislation exists to protect the rights of incapacitated adults that made unbiased research into sudden brain injury impossible until trumped on 1 May 2004 by the implementation of the European Clinical Trials Directive, which makes it (more or less) possible again, although problems remain.[7–9] In England, but not in Scotland, the research use of routinely collected health data is regulated by legislation under section 60 of the Health and Social Care Act,[10] but, illogically, audit escapes almost any regulation at all. Not surprisingly, much research is now conveniently rebadged as audit.

So what is worrying the researchers this week? Hester Ward and colleagues describe how their case-control study in Creutzfeldt-Jakob disease has been made extremely complicated and expensive by the demands of modern data protection.[1] Worse, their methods are now so severely compromised that the response rate among the controls is only a meagre 16%, and so the results are likely to be unreliable. Konrad Jamrozik bemoans the length and complexity of research ethics committee review and makes suggestions for improvement.[2] As of 1 March 2004 the new arrangements are meant to be an improvement on the old, but with a 68 page form, with one extra for student projects, Wald remains unconvinced.[4] The questions are very little to do with ethics, and for his own simple project the form required 44 hours to complete, at a cost of about £850. Jones and Bamford describe their dismay when they discovered that apparently trivial (to the investigators) changes in their protocol had to go back for a lengthy approval process by the ethics committee and R&D department, and every other project in their unit was scrutinised as well.[3] And finally, Michael Parker and colleagues try to sort out just what is research and so requiring ethics committee approval, and what is clinical practice when it comes to investigating rare genetic disorders—another minefield for the unwitting researcher.[5]

These are increasingly familiar problems and a threat to the future of clinical research.[11] Rightly or wrongly, clinical researchers are exhausted by the demands of ethics committees that seem more concerned with the science (which they cannot necessarily judge) and editorial control of patient information sheets than with ethics. But what can be done? The epidemiologist Sir Richard Doll has been quoted as saying that no one with the power to do anything will take any notice until a bona fide researcher is jailed for transgressing some trivial regulation, and he sportingly volunteered to be the test case himself.[12] Others have suggested that we must involve patients and patients' organisations. After all government is more likely to listen to consumers, in this case of research findings, than researchers. In the meantime, when discussing any flaws in their study, researchers should make plain which scientifically inappropriate aspects of the methods were forced on them by ethics committees and how the results may be biased as a consequence. If nothing is done, clinical research will wither, and that is not to anyone's advantage.

Charles Warlow *professor*

Department of Clinical Neurosciences, Western General Hospital, Crewe Road, Edinburgh EH4 2XU

(charles.warlow@ed.ac.uk)

Competing interests: CW is a member of the Royal College of Physicians (London) committee on ethical issues in medicine and the MRC committee on the ethics of research involving human participants or tissues and personal information, but the views in this paper are his own. His recent application to a research ethics committee for a student project was turned down and is currently subject to appeal.

1 Ward HJT, Cousens SN, Smith-Bathgate B, Leitch M, Everington D, Will RG, et al. Obstacles to conducting epidemiological research in the UK general population. *BMJ* 2004;329:277-9.
2 Jamrozick K. Research ethics paperwork: what is the plot we seem to have lost? *BMJ* 2004;329:286-7.
3 Jones AM, Bamford B. The other face of research governance. *BMJ* 2004;329:280-1.

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4 Wald DS. Bureaucracy of ethics applications. *BMJ* 2004;329:282-4.
5 Parker M, Ashcroft B, Wilkie AOM, Kent A. Ethical review of research into rare genetic disorders. *BMJ* 2004; 329:288-9.
6 Wichman A, Sandler AL. Research involving critically ill subjects in emergency circumstances: new regulations, new challenges. *Neurology* 1997;48:1151-77.
7 Scottish Executive. Adults with incapacity (Scotland) Act 2000. Code of Practice. For persons authorised to carry out medical treatment or research under part 5 of the Act. 2002.
8 Directive 2001/20/EC of the European Parliament and of the Council of 4th April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. *Official Journal of the European Communities* 2001; L121:34-44. http://europa.eu.int/eur-lex/pri/en/oj/dat/2001/l_121/l_12120010501en00340044.pdf (accessed 22 Jul 2004).
9 Nicholson R Another threat to research in the United Kingdom *BMJ* 2004;328:1212-3.
10 Health and Social Care Act 2001, Part 5, Miscellaneous and Supplementary, section 60.
11 Academy of Medical Sciences. *Strengthening clinical research. A report from the Academy of Medical Sciences. October 2003.* London: Academy of Medical Sciences, 2003. www.acmedsci.ac.uk/p_scr.pdf (accessed 22 Jul 2004).
12 Fazackerley A. Top cancer expert, 91: "I'll go to jail for science". *Times Higher Education Supplement*, 27 February 2004.

Travelling but never arriving: reflections of a retiring editor

Twenty five years of adventure, discovery, and conservatism

When I arrived at the *BMJ* in 1979 the journal was set in hot metal, there wasn't a computer to be seen, and it took three months for copies of the journal to reach Australia. As I depart a quarter of a century later, many more people access the journal through their computers than on paper, and Australians are the first to read each issue because the British are abed when it hits their screens. Yet my overwhelming impression is that change has been slow. If resurrected, Thomas Wakley, the founder of the *Lancet* who died in 1862, would instantly recognise both his journal (despite its recent makeover) and the *BMJ*. We are still at the beginning of the electronic revolution, and Drummond Rennie, the deputy editor of *JAMA*, has castigated editors for neglecting their craft and failing to innovate.[1 2] We have been an instinctively conservative crew.

It took me many years to realise that I completely misunderstood what journals did. I imagined that doctors opened their *BMJ*s on Friday mornings, read of some innovation, and used it on the next relevant patient. Many still seem to cling to this naive view of the function of journals. In fact words on paper rarely lead directly to change—and thank goodness they don't, considering the rubbish that journals often publish.[3] What journals do best is what the rest of the media do best: stir up, prompt debate, upset, probe, legitimise, and set agendas. They are good at telling readers what to think about but not what to think, and theme issues may be particularly successful in putting important but neglected subjects to doctors. Increasingly I wonder as well if there isn't something fundamentally misguided in sending ordinary clinicians, who are not scientists, piles of original papers that they mostly don't read, often aren't relevant to them, and they are not trained to appraise.[4] If we were clearer about the purpose of journals then we might redesign them completely.

Slowly the content of journals is shifting from being mostly original studies (with only about 1% of them both valid and relevant to clinicians[3]) to being more educational, review, newsy, and debate material—material that doctors actually read. But it's slow because current business models work against the shift: publishers such as the infamous Robert Maxwell, who was found naked and dead in the Atlantic in 1991, have become rich by selling value added by others (researchers) at high prices and keeping their costs to a minimum.

The Robert Maxwells of this world have infuriated the academic community with their business model of compensating for declining subscriptions by annually increasing prices above inflation. I call this the "pay more, get less" model, and it couldn't be sustained. It spawned the "open access" movement, which aspires for all research, most of it funded with public money, to be available free to all on the web. I've been arguing for nearly a decade that this had to happen, and, interestingly, in the fortnight before I step down a parliamentary committee in Britain has called for open access and, more powerfully, a house committee in the United States has said that all research funded by the National Institutes of Health should be published in open access journals.[5–6] Although we will start charging for access to bmj.com in January, the original research articles will continue to be free and be passed directly to Pubmed Central. The *BMJ* is thus an open access journal. (I will be able to continue my interest in this subject as I am joining the board of the Public Library of Science, which wants all research to be available to all for free and will in the autumn launch the new journal *PLoS Medicine*.)

The scientific value of the original studies published in journals has improved a little over the past 25 years as case reports and series have given way to randomised trials (albeit, most of them too small and badly done and reported[7–9]), but most medical journals have kept to a narrow methodological range. Believing that the many questions of health and health care need many methods, we have tried with the *BMJ* to broaden our range into qualitative research, economic evaluations, ethnographic studies, modelling papers, and quality improvement reports—but it's scientifically perilous getting to grips with new methods.

The forms of the *BMJ* have developed dramatically in the past quarter century. bmj.com—which appeared in 1994, when websites were numbered in thousands rather than tens of millions—is the finest flowering of the *BMJ* so far—but we are still in the journal equivalent of the early days of film: the talkies have yet to appear. The site being free to all has, I think, hugely increased the influence and usefulness of the journal. The *studentBMJ*, "the *BMJ* on speed," is a child of whom I

BMJ 2004;329:242–4