

Time to assume that health research is fraudulent until proven otherwise?

By Richard Smith, 31 August 2022

Health research is based on trust. Health professionals and journal editors reading the results of a clinical trial assume that the trial happened and that the results were honestly reported. But about 20% of the time, said Ben Mol, professor of obstetrics and gynaecology at Monash Health, they would be wrong. As I've been concerned about research fraud for 40 years, I wasn't that surprised as many would be by this figure, but it led me to think that the time may have come to stop assuming that research actually happened and is honestly reported, and assume that the research is fraudulent until there is some evidence to support it having happened and been honestly reported. The Cochrane Collaboration, which purveys "trusted information," has now taken a step in that direction.

As he described in a webinar last week, Ian Roberts, professor of epidemiology at the London School of Hygiene & Tropical Medicine, began to have doubts about the honest reporting of trials after a colleague asked if he knew that his systematic review showing the mannitol halved death from head injury was based on trials that had never happened. He didn't, but he set about investigating the trials and confirmed that they hadn't ever happened. They all had a lead author who purported to come from an institution that didn't exist and who killed himself a few years later. The trials were all published in prestigious neurosurgery journals and had multiple co-authors. None of the co-authors had contributed patients to the trials, and some didn't know that they were co-authors until after the trials were published. When Roberts contacted one of the journals the editor responded that "I wouldn't trust the data." Why, Roberts wondered, did he publish the trial? None of the trials have been retracted.

Later Roberts, who headed one of the Cochrane groups, did a systematic review of colloids versus crystalloids only to discover again that many of the trials that were included in the review could not be trusted. He is now sceptical about all systematic reviews, particularly those that are mostly reviews of multiple small trials. He compared the original idea of systematic reviews as searching for diamonds, knowledge that was available if brought together in systematic reviews; now he thinks of systematic reviewing as searching through rubbish. He proposed that small, single centre trials should be discarded, not combined in systematic reviews.

Mol, like Roberts, has conducted systematic reviews only to realise that most of the trials included either were zombie trials that were fatally flawed or were untrustworthy. What, he asked, is the scale of the problem? Although retractions are increasing, only about 0.04% of biomedical studies have been retracted, suggesting the problem is small. But the anaesthetist John Carlisle [analysed 526 trials submitted to *Anaesthesia*](#) and found that 73 (14%) had false data, and 43 (8%) he categorised as zombie. When he was able to examine individual patient data in 153 studies, 67 (44%) had untrustworthy data and 40 (26%) were zombie trials. Many of the trials came from the same countries (Egypt, China, India, Iran, Japan, South Korea, and Turkey), and when John Ioannidis, a professor at Stanford University, [examined individual patient data from trials](#) submitted from those countries to *Anaesthesia* during a year he found that many were false: 100% (7/7) in Egypt; 75% (3/4) in Iran; 54% (7/13) in India; 46% (22/48) in China; 40% (2/5) in Turkey; 25% (5/20) in South Korea; and 18% (2/11) in Japan. Most of the trials were zombies. Ioannidis concluded that there are hundreds of thousands of zombie trials published from those countries alone.

Others have found similar results, and Mol's best guess is that about 20% of trials are false. Very few of these papers are retracted.

We have long known that peer review is ineffective at detecting fraud, especially if the reviewers start, as most have until now, by assuming that the research is honestly reported. I remember being part of a panel in the 1990s investigating one of Britain's most outrageous cases of fraud, when the statistical reviewer of the study told us that he had found multiple problems with the study and only hoped that it was better done than it was reported. We asked if he had ever considered that the study might be fraudulent, and he told us that he hadn't.

We have now reached a point where those doing systematic reviews must start by assuming that a study is fraudulent until they can have some evidence to the contrary. Some supporting evidence comes from the trial having been registered and having ethics committee approval. Andrew Grey, an associate professor of medicine at the University of Auckland, and others have developed a checklist with around 40 items that can be used as a screening tool for fraud (you can [view the checklist here](#)). The REAPPRAISED checklist (Research governance, Ethics, Authorship, Plagiarism, Research conduct, Analyses and methods, Image manipulation, Statistics, Errors, Data manipulation and reporting) covers issues like "ethical oversight and funding, research productivity and investigator workload, validity of randomisation, plausibility of results and duplicate data reporting." The checklist has been used to detect studies that have subsequently been retracted but hasn't been through the full evaluation that you would expect for a clinical screening tool. (But I must congratulate the authors on a clever acronym: some say that dreaming up the acronym for a study is the most difficult part of the whole process.)

Roberts and others wrote about the problem of the many untrustworthy and zombie trials in *The BMJ* [six years ago](#) with the provocative title: "The knowledge system underpinning healthcare is not fit for purpose and must change." They wanted the Cochrane Collaboration and anybody conducting systematic reviews to take very seriously the problem of fraud. It was perhaps coincidence, but a few weeks before the webinar the Cochrane Collaboration [produced guidelines on reviewing studies](#) where there has been a retraction, an expression of concern, or the reviewers are worried about the trustworthiness of the data.

Retractions are the easiest to deal with, but they are, as Mol said, only a tiny fraction of untrustworthy or zombie studies. An [editorial in the *Cochrane Library*](#) accompanying the new guidelines recognises that there is no agreement on what constitutes an untrustworthy study, screening tools are not reliable, and "Misclassification could also lead to reputational damage to authors, legal consequences, and ethical issues associated with participants having taken part in research, only for it to be discounted." The Collaboration is being cautious but does stand to lose credibility—and income—if the world ceases to trust Cochrane Reviews because they are thought to be based on untrustworthy trials.

Research fraud is often viewed as a problem of "bad apples," but Barbara K Redman, who spoke at the webinar insists that it is not a problem of bad apples but bad barrels if not, she said, of rotten forests or orchards. In her book *Research Misconduct Policy in Biomedicine: Beyond the Bad-Apple Approach* she argues that research misconduct is a systems problem—the system provides incentives to publish fraudulent research and does not have adequate regulatory processes. Researchers progress by publishing research, and because the publication system is built on trust and peer review is not designed to detect fraud it is easy to publish fraudulent research. The business model of journals and publishers depends on

publishing, preferably lots of studies as cheaply as possible. They have little incentive to check for fraud and a positive disincentive to experience reputational damage—and possibly legal risk—from retracting studies. Funders, universities, and other research institutions similarly have incentives to fund and publish studies and disincentives to make a fuss about fraudulent research they may have funded or had undertaken in their institution—perhaps by one of their star researchers. Regulators often lack the legal standing and the resources to respond to what is clearly extensive fraud, recognising that proving a study to be fraudulent (as opposed to suspecting it of being fraudulent) is a skilled, complex, and time consuming process. Another problem is that research is increasingly international with participants from many institutions in many countries: who then takes on the unenviable task of investigating fraud? Science really needs global governance.

Everybody gains from the publication game, concluded Roberts, apart from the patients who suffer from being given treatments based on fraudulent data.

Stephen Lock, my predecessor as editor of *The BMJ*, became worried about research fraud in the 1980s, but people thought his concerns eccentric. Research authorities insisted that fraud was rare, didn't matter because science was self-correcting, and that no patients had suffered because of scientific fraud. All those reasons for not taking research fraud seriously have proved to be false, and, 40 years on from Lock's concerns, we are realising that the problem is huge, the system encourages fraud, and we have no adequate way to respond. It may be time to move from assuming that research has been honestly conducted and reported to assuming it to be untrustworthy until there is some evidence to the contrary.

Richard Smith was the editor of The BMJ until 2004.