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

July 5, 2021

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 None of the trials have been retracted.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 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.*

Competing interest: RS was a cofounder of the Committee on Medical Ethics (COPE), for many years the chair of the Cochrane Library Oversight Committee, and a member of the board of the UK Research Integrity Office.

Richard Smith

« Alcohol health labelling is needed urgently—the Government must act

Trish Greenhalgh: Freedom Day, but at what cost? »

C **Cartesianwell**

3 years ago

Having this year, been in part driven into early retirement by uncovering cheating in doctoral research which others wanted buried, I have little reason to doubt that fraud of one sort or another is not restricted to my own former institution.

6 0 Reply

L **lynngeek77** Cartesianwell

3 years ago

The whistle-blowers mentioned in the 1978 NOVA program "Do Scientists Cheat" all regretted reporting the fraud they observed because their reward was receiving worse treatment than the cheaters. All of them said that they would never report another case of fraud.

6 0 Reply

jamadaniel

3 years ago

The impact of the problem is that thanks to the pandemic and the never-ending cycle of conflicting studies has revealed the dysfunction to the masses. No one trusts doctors or scientists anymore.

7 0 Reply

Eric H

3 years ago

What do we have here? Yet another "Independent" Fact Checker in the making? What we need are fewer fact checker and less

censorship. Also get rid of the conflict of interest that arises by the incestuous relationship between scientific journals and the (deep pocketed) institutions that fund and promote the research.

4 0 Reply

J

Jim Zero

3 years ago

Margarine is still said to be healthier than butter. Why believe anything?

6 0 Reply

C

CC7

3 years ago

I haven't trusted 'science' for a long time and this comes as no surprise to me. The pharmaceutical sector have been fudging their research for decades. It is cheaper for them to pay the fines when caught than to be honest. Furthermore, they are legally obliged to maximise returns to shareholders (due to their corporate nature) but have no obligation at all to improve public health. Hence the more we spend on health, the worse public health continues to get. Time pharmaceutical companies had their dollar backed power taken from them.

7 0 Reply

Nagora → CC7

3 years ago

The answer to "they are legally obliged to maximise returns to shareholders (due to their corporate nature) but have no obligation at all to improve public health" is that the law should utterly crush companies that engaged in fraud - invalidate or seize patents, set price caps, nationalise research centres, jail management. That makes the shares fall in value and suddenly the company has an obligation to improve health because otherwise they are not maximising returns to shareholders.

It's not hard to think of ways to leverage "maximise returns to shareholders" to align it with public health. We just need someone with the guts to implement it.

2 0 Reply

grumpy

3 years ago

Awesome article.
I think it's important to note that fraud isn't done because people enjoy lying, or because they just want to get published. There is often a profit motive. Sorting out the financial incentives is an

important and often overlooked part of critical thinking. Scientists like to assume they are above all that... Doctors try not to know the price of medications they prescribe "as long as it's covered by insurance". But it's really bad for patients and researchers to ignore the bias created by the industry.

6 0 Reply

Nativist → grumpy

3 years ago

The "profit" is often psychological, not monetary. *"Follow the money"* is NOT a good guide. Many people will cross ethical boundaries for approbation, revenge, through psychopathic tendencies - or perhaps because they get a buzz from taking a self-destructive risk (like a "flasher").

5 0 Reply

jamadaniel → Nativist

3 years ago

Don't be so fast to write off the most powerful motive of all ... studies that support a revenue stream. Most climate science these days is driven by cash as well. Why would health science be any different.

9 0 Reply

J

Joseph Kane

3 years ago

REAPPRAISED is an acrostic poem. It's not an acronym. It's not even an abbreviation. It's an acrostic poem. And I am terribly irked by how they've penetrated our corporate, academic, and governmental parlance.

1 0 Reply

Jason Harrison → Joseph Kane

3 years ago

The other accepted name for this is an initialism. Like ISO, NASA, IRS, EU, USA, ROC, COPE, UK...

While too many of them can create confusion and make the writer or source sound more reliable and trusted than they should be, they are also an accepted way in many industries to standardize the terms used to specify what we're referring to. Should we refer to the "Grey et al 2020 checklist" or the "REAPPRAISED checklist 2020"?

0 0 Reply

js290

3 years ago

"medical studies funded by Pharma... their motive is wealth, not health..." -Ron Rosedale

14 0 Reply

P

PeteB

3 years ago

For those not familiar with the term, 'zombie trails' refers to trails where the individual data or statistics blatantly lacks credibility or is inconsistent.

4 0 Reply

JerryTK214

3 years ago

While not a topic in this article, fraud for political purposes is also rampant in medical and scientific study. It is becoming impossible to 'trust' the science when so much of it is lies and deceit.

12 0 Reply

grumpy

3 years ago

Awesome article. With unfortunately the huge blind spot, typical for medical researchers. Fraud isn't done because people enjoy lying, or because they just want to get published. There is a profit motive. The #1 source of bias in research that dwarfs all others is the profit motive, for one of the bigger industries, Big Pharma. That also drives researchers to do things to please the operators of the "revolving door" that will employ them in the future when they leave their govt or university post. Imagine a conversation like "We should hire that guy- his paper helped sell $1.2 billion in molnupiravir."

The FDA's anti-Fraud effort is working at full speed- in Reverse!
Their duty is to protect the public purse and patients from side-effects.
They are effective against expensive and profitable drugs with rich sponsors that don't work... (mostly).
But they are killing us by stopping entirely the re-purposing of inexpensive drugs.
You can't blame FDA or Frankenstein for the ugly way they are built. Congress only allows studies to be sponsored by for-profit corporations. No company can reasonably be expected to send millions of $, to make thousands, while taking on billions in liability and missed opportunity cost.
So FDA stops cold efforts to use cheap drugs with proven ability to prevent COVID disease, even when huge trials show they work. See FLCCC for example

Instead of protecting us from expensive drugs that don't work or are dangerous, they are protecting us from cheap safe drugs with a 30 year safety track record, and billions of doses administered. That protection racket lets people come in with a new patent medicine that's less effective but 100x as expensive, such as Molnupiravir, to displace the generic alternative. We can expect that a $1.2 billion dollar initial sale indicates there should be, according to business practice, around $24 million in PR budget. That's enough to give street walking money to a lot of comely sales reps.

14 0 Reply

Eric Lang

3 years ago

Can we trust the veracity of what's reported in this article about the incidence of research fraud, or assume it's wrong until proven otherwise?

6 7 Reply

tom → Eric Lang

3 years ago

What advantage (financial or otherwise) would the author stand to gain from making fraudulent statements?

He is likely to have made a lot of rich and powerful enemies; if his statements were shown to be false, his reputation would be damaged as well.

9 0 Reply

Opinionated → tom

3 years ago edited

Publish or perish . . .

Plus, most simply take the study at face value. Even though the authors are supposed to provide the raw data to those who ask, very few ever ask.

1 0 Reply

L

lynngeek77 → Opinionated

3 years ago

The driving mantra when I was in grad school in the late 1960's. I waited for weeks on pins and needles hoping that no other paper published my conclusions before my paper was printed. Otherwise I would have had to

start over.

1 0 Reply

William Norton Eric Lang

3 years ago edited

Pure deflection. No one making positive assertions about drugs, treatment, etc. in this article. And by engaging in this sophistry you quite conveniently don't have to talk about the real problem, right?

14 0 Reply

Cochrane Injuries

3 years ago

A recording of the webinar has been posted here: Fraudulent Trials in Systematic Reviews - A Major Public... – disq.us

6 0 Reply

lburkefiles

3 years ago

As long as the incentives are perverse and there are no adults in the room, this will be the norm.

I have chased fraud for over 30 years. First perverse incentives. Suppose you get paid for taking risks and being successful. That is ok. It is not ok if you get rewarded even when you fail. In science, progress is incremental, and knowledge is the measuring stick. Most only write and publish if their data supports their hypothesis. Thus there is often a lot of “selection pressure” on the data looking for confirmation. If a hypothesis is wrong - that too is knowledge and should be published.

Now, what if the research was fabricated? Honestly, there are so few penalties it makes economic sense to fake the data. The funders of research are investors in an outcome and expect a dividend of knowledge. If they are defrauded - they need to go after the research team for a full refund plus a penalty - just like when you defied a stock investor. Privatizing gains in research and socializing the exposed fraud to the funders’ wallets of the research program is a recipe for more fraud.

Researchers are no more and no less honest than public company CEOs, plumbers, or electricians. Yet, where is the third-party supervision? CEOs have auditors and the trades have building inspectors. Where are the independent minds for oversight in research? The oversight has always been needed. Brian Nosek’s reproducibility project rubbed the amount of fraud and error in everyone’s face. With only 1/3 of the published studies they reviewed were reproducible and down 10% produced a statistically

significant result - that was the wake-up call. Folks, there was no adult in the room.

Retraction Watch continues this most valuable work in crafting a vital tool of a searchable database of retracted papers and a rogues gallery of dodgy researchers.

I work with companies and funders assessing new technology. The first two steps are check Retraction Watch and see if the results have been independently reproduced. If the study or its authors are in RW or cited a paper in RW after it had been retracted. The study is ignored. If the study has not reproduced - it is at best only a hunch.

The assumption all research is fraudulent; I'll not go that far. There are also honest errors and sample size problems. However, one must be diligent in accepting all-new research. If it is reproducible and its processes can pass an audit - well, then I am all ears.

20 0 Reply

J **John Moffett** lburkefiles

3 years ago

I noticed this problem beginning in the 1990s when the NIH shifted from funding basic research to "translational" research. Once it became a business endeavor aimed at IP development, rather than an attempt to understand biology, things went downhill. This will not get fixed by regulation, it will get fixed by more funding of basic science. Diverting 5% of the military budget (the bulk of discretionary spending) to the NIH would double NIH funding and allow many more labs to conduct research. As it is now, many smaller labs are starved for funding, and the larger labs that strive for IP drug development are over-funded.

7 0 Reply

Opinionated John Moffett

3 years ago

Perhaps but not without major oversight. It is too easy to "fund" pet projects.

Also, once the funds get to where they are going, oversight needs to happen there as well to make sure the money is spent for it's specified purpose.

And there needs to be scientific oversight as well to make sure the studies are well designed & executed. Verification of subjects and results as well as data analysis need to be closely

followed.

Just funding basic research will not take care of fraud.

1 0 Reply

L

lynngeek77

Opinionated

3 years ago edited

"Scientific Oversight" is easy to demand but may be impossible to implement. The problem is international but another UN panel would make the problem worse. So would a national agencies, regardless of the party in power.
It's obvious that neither universities or publishers have the will (or morals?) to self-regulate. Peer reviews have failed and Replication studies won't be funded.
It is so bad now that some fraudsters are publishing in Academia.edu, which has that reserved domain extension because it was grandfathered in, and many who read those works of fiction don't know that.

What is missing, and has little hope of being restored is the honest scientist. I

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