

Written Evidence Submitted by Dr Peter Wilmshurst

(RRE0099)

Summary

There can be honest reasons for failure to replicate medical research, such as when slight differences in experimental conditions result in different outcomes. That can occur if the initial report did not provide complete and precise experimental details or because of biological variation between the patients who were the subjects in each set of experiments. Failure to replicate may be also the result of research misconduct.

When there is a failure to replicate research only subsequent research can determine whether the original findings or the data from the replication experiments are correct. Concordance between original and replication experiments is reassuring, but it can provide false reassurance if both original and replication experiments produced incorrect data. Such concordance of incorrect original data and incorrect replication experiments may be the result of research fraud because often a fraudster believes that fabricating results to accord with the expected findings or published data are good ways to avoid detection.

Many reports of failure to replicate are never published because journals, sponsors and academic institutions have vested interests in preserving the impression that science is precise and scientists are universally competent and honest. Much original data that should be confirmed is not subject to replication experiments because scientists realise that they will gain little credit from performing replication experiments and they will have great difficulty getting their findings published.

I will provide some personal experiences and suggested remedies.

My reasons for concerns about failure to replicate research

1. I have worked as a doctor in the NHS since 1974. I am currently a consultant cardiologist. Therefore I realise the necessity to have clinical trial results that can be replicated so that they are generally applicable to the treatment of patients.
2. For more than 40 years I have undertaken and published medical research. In general my research has been replicated by others. I have also performed a number of replication experiments on research when I was concerned that the reported findings were likely to be incorrect and I had great difficulty getting journals to publish my reports of failure to replicate experiments. What I found most worrying was that the journals that published the original data that I was unable to replicate consistently refused to publish my failures of replication even though in every case I had performed considerably more observations than in the original reports because I wanted to be sure of my findings.
3. I have investigated research misconduct in the UK and overseas for nearly 40 years. I have reported more than 25 doctors to the General Medical Council (GMC). As a result some dishonest doctors have been removed from the UK Medical Register. One doctor that was suspended from the Medical Register for research fraud after I reported to the GMC illustrates a problem: his fraudulent claims in a major medical journal to have data

confirming findings reported by Dr Andrew Wakefield has not been retracted years after the GMC suspended him from the Medical Register for fabricating those data.

4. I teach medical students and post graduate doctors and I frequently lecture about dishonesty in medical research.

My experience

1. I was the principal investigator in a replication study on a drug used to treat patients with cardiac failure. Our study had many more patients than in the original research. Our findings entirely refuted the original claim that the drug was beneficial. In fact the drug increased adverse events and patient mortality. The pharmaceutical corporation that made and marketed the drug offered me a large bribe (equivalent to my salary for two years) not to publish our findings, which I rejected. They then threatened litigation in an attempt to get me not to publish our failure to replicate the original data. The earlier study that we failed to replicate was performed by cardiologists who were paid consultants to the corporation, but the financial conflicts of interest were not disclosed in the publication. Our findings reduced the marketability of the corporation's product. When our findings were eventually published the drug was withdrawn World-wide.
2. When I presented our data at scientific meetings, medical opinion leaders (with financial links to the corporation) repeatedly claimed that they had tried and failed to replicate our experiments. Decades later, none has published a paper refuting our observations, which suggests that their claims to have failed to replicate our findings were false attempts to discredit our research.
3. Over many years I have experienced difficulty in getting reports of failure to replicate research published in journals. I believe that usually was because reports of failure to replicate do not bring income to the publishers, but in some cases editorial conflicts of interest were apparent.
4. There can be false claims to have replicated original research. In my experience this happened because fraudsters fabricated the replication experiments believing that their misconduct will not be suspected if their data are concordant with earlier observations. I have been involved in two large investigations of fraudulent replication experiments. In both cases the research had implications for patient survival. In one case, I chaired an inquiry that found that fraudsters made up data so that it was in complete agreement with other research that was genuine and valid. In the other case, I was a member of an inquiry panel that found research fraudster had pocketed \$5 million in grants by making up data consistent with earlier research, which also proved to be fabricated.

Suggested remedies

1. There needs to be better recognition that research misconduct, particularly in medical research, puts the general public at risk and that it wastes public finances because grants are misused and false publications causes other researchers to follow incorrect research paths.
2. There needs to be recognition that replication experiments are important for detecting poor quality and fraudulent research. Therefore replication experiments should be encouraged.
3. We need ways of publishing replication experiments, regardless of whether they are confirmatory or contradictory, and those who do such research should get adequate

recognition and reward. I am not sure how this can be done when sponsors, academic institutions and journals do not encourage people to do replication experiments. A possible way, when research is used to obtain a product licence for marketing a drug or medical device, would be for licencing agencies to grant only provisional marketing approval until data from replication experiments are produced when the product would receive confirmation of a product licence. But that would not solve the problem for most research, which is not used for licencing.

4. It is clear that the existing mechanisms for investigation of research misconduct do not work. Academic institutions and hospitals consistently try to conceal misconduct in their institutions. UKRIO appears unwilling to investigate research misconduct in universities and has no authority over hospitals, where most UK clinical research occurs. Industry sponsors do not want misconduct investigated. Grant awarding charities and government bodies do not want public recognition that they have wasted large amounts of money on fraudulent research. Journals do not want readers to realise how much fraud and poor science they publish. Therefore we need an independent national body to investigate allegations of research misconduct. The organisation should have trained specialist investigators comparable to police specialist art and financial fraud squads and the Health and Safety Executive. They should have legal authority to compel individual researchers and academic institutions to cooperate and produce documents and data when demanded. However, even a national body might have difficulty investigating misconduct when researchers collaborate with colleagues in other countries.
5. Serious research misconduct should be dealt with in criminal courts, not by bodies such as the GMC. When patients are harmed by dishonest research or a significant amount of money is wasted, those responsible should face criminal sanction, which are similar to the sanction for comparable physical assaults or financial frauds. In addition, criminal courts could deal with research misconduct by non-medical scientists. Academic institutions, hospitals and managers that cover up misconduct should face punitive sanctions, which might include large fines and orders to repay misused grants.

(February 2022)