Historical Reflections on the Prosecution of Research Fraud

Dr Frank Wells

Vice Chairman, Cambridgeshire 4 Research Ethics Committee, UK
Co-Founder and former Medical Director, MedicoLegal Investigations

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Historical Reflections on the Prosecution of Research Fraud

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Ideally, fraud should not occur at all

BUT

We do not live in an ideal world
On June 28, 2006, Poehlman was ordered to serve a year and a day in a federal prison for using falsified data in federal research grants that he submitted for funding.

In addition to jail time, Poehlman will be permanently barred from getting more federal research grants, and was ordered by the court to write letters of retraction and correction to several scientific journals.
Korean stem-cell case, Woo-suk Hwang

Who Is Telling the Truth?
Hwang Defends Stem Cell Work; Coauthor Repeats Fabrication Claim

By Kim Tae-kyou
Staff Reporter

Korea’s cloning scientist Hwang Woo-suk contended his team did create several tailor-made stem cells and will prove the authenticity of the medical potential-laden cells in about 10 days.

During a press conference Friday at Seoul National University Hospital, Hwang apologized for disputes over the stem cell research and said he had requested the withdrawal of the stem cell paper in question featured by U.S. journal Science in May.

However, the 52-year-old geneticist rebuffed the claim of his close aide Roh Sung Il, head of Haneul Women’s Hospital, who argued on Thursday that Hwang admitted the stem cells were fake.

Jon Sudbø, Norwegian Radium Hospital, Oslo

Research scam makes waves

A Norwegian doctor’s fabrication of cancer research is making waves far beyond Norway’s borders. The fraudulent research may have led to faulty treatment of cancer patients, international investigations have been launched into how the fraud could have occurred, and top Norwegian officials all the way up to the ministerial level are desperately trying to control the damage.

The editor of the respected magazine, The Lancet, in which the fabricated article was published, calls the fraud “the worst the research world has seen.”

Richard Horton told Oslo newspaper Aftenposten that he also can’t understand how the Oslo doctor’s 13 co-authors and colleagues on the fraudulent cancer research project could have been duped as well.

Horton claims at least six of the doctor’s co-authors corresponded with The Lancet, and were highly involved with the substance of the article.

Richard Horton, editor of The Lancet, is furious that a Norwegian doctor duped his publication. He insists all editorial controls were in place.

Health Minister Sylvia Brustad is expected to pay more attention now to proposals aimed at thwarting research cheats.

PHOTO: THE LANCET
September 2009

“Professor to face GMC over his claim to have seen full trial data” Clare Dyer BMJ 2009;339:b3990

“Indian investigator suspended for alleged fraud” CRFocus 9 September 2009 p14: www.icr-global.org/resources/news/?entryid23=5451

What are we really talking about?
The Definition of Research Misconduct:
“Behaviour by a researcher, intentional or not, that falls short of good ethical and scientific standards”

Clinical research fraud is best defined as:

*The generation of false data with the intent to deceive*
The Prevalence of Clinical Research Fraud

….. is difficult to assess
My own estimate is that it is at least 1% but probably higher and possibly much higher
If we estimate that there are about 4,000 sponsored clinical research projects taking place within Europe at any one time, this means that at least 40 will include investigators who are generating false data
The FDA estimates 4 to 5% (2009).

Prevalence of Fabrication and Falsification

It is likely that, if an average 2% of scientists admit to having falsified research at least once and 34% admit to other questionable research practices, the actual frequencies of misconduct could be higher than this. Fanelli D, Institute for the Study of Science, Technology and Innovation, University of Edinburgh (2009)
But attempts at detection are difficult due to the thin line separating intentional misconduct and carelessness.
Cases of Research Fraud Referred to the UK General Medical Council in the last decade:

- Number referred: 28 (+3)
- Number found guilty of serious professional misconduct: 27
- Number admonished: 4
- Number whose registration made conditional: 2
- Number suspended: 6
- Number erased from the medical register: 15

COPE is a forum for editors of peer-reviewed journals to discuss issues related to the integrity of the scientific record; it supports and encourages editors to report, catalogue and instigate investigations into ethical problems in the publication process.

Formed in 1997, the Committee on Publication Ethics' (COPE) major objective is to provide a sounding board for editors who were struggling with how best to deal with possible breaches in research and publication ethics.
Problems/dilemmas discussed*

- Duplicate/redundant publication 58
- Authorship issues 26
- No ethics approval 25
- No or inadequate informed consent 22
- Falsification or fabrication 19
- Plagiarism 17
- Unethical research or clinical malpractice 15
- Undeclared conflict of interest 8
- Reviewer misconduct 6
- Editorial misconduct 3
- Other 39

*More than one possible

Retractions

Retractions in the biomedical literature are more than twice as likely to result from unintentional mistakes than from scientific misconduct Nath SB et al Med J Aust 2006; 185; 152-4
Some wrong reasons why investigators choose to do research:

(i) Pressure to publish - at all costs
(ii) Pressure by sponsors
(iii) Greed
(iv) Vanity or arrogance
(v) Sheer boredom of routine clinical practice
(vi) Emotional disturbance or mental illness
(vii) etc. etc.

Prevalence v Prosecution

Fear of………………
  recrimination
  adverse publicity,
  loss of favour and support
  loss of commercial status
  getting it wrong

Don’t know what to do
Research Misconduct in the Nordic Countries

Despite a widely recognised need, most countries still have no coherent system to deal with scientific misconduct. BUT, Committees *have* been established by the national medical research councils in Denmark (1992), Norway (1994), and Sweden (1997), and by the Ministry of Education in Finland (1994), to deal with scientific misconduct—i.e., to initiate preventive measures, to investigate alleged cases, or both. Each committee includes both scientifically and legally qualified members. The employing institutions are responsible for possible sanctions or punishments.

France

In France, the notion of fraud was only conceptualised in general legislative texts which covered all activities (e.g. civil or criminal law). Silence was generally the official and professional golden rule. *(Husson and Demarez, 2001)*

But maybe things are about to change?
German Case Not Taken to Court

In 2000, a task force of scientists engaged by the German Research Foundation concluded that 94 out of 347 research papers published by a professor from the University of Lubeck contained manipulated data. But agreement was reached that he should make a minor payment and then that his guilt was to be labelled as negligible, as repetition was unlikely and public interest was small.

Tuffs A. BMJ 2004; 328: 544 (6 March)

South Africa

The Bezwoda case

(but the prevalence of clinical research misconduct is unknown)
Australia
The MacBride case
The Whistleblowers Handbook

(but the prevalence of clinical research misconduct is unknown and there is no formal mechanism in place)

Belgium
Ireland
Italy
The Netherlands
Spain
Portugal
Switzerland
Canada
New Zealand
South America
Eastern Europe

The prevalence of clinical research misconduct is unknown and there is no formal mechanism in place
The UK Research Integrity Office (UKRIO)

The aim is to provide a comprehensive service in support of research integrity to the health and biomedical sciences research community.

A key element of the service will be access to a Register of Advisers, experts in systems for research management to promote good conduct, and those with experience in investigating allegations of misconduct.

Examples of cases considered

A general practitioner fabricated research ethics committee approval, twice. Erased from the Medical Register.

A second general practitioner committed suicide after, amongst other fraudulent activities, forging REC approval.

An academic consultant in respiratory medicine forged REC approval twice for the same study. Admonished and registration conditional upon his conducting subsequent research under supervision.
Examples of cases considered

An academic consultant surgeon conducted two studies at once on the same patients without ethics committee approval. Found guilty of serious professional misconduct and admonished.

Another academic consultant surgeon purported to have assessed a patient in a study for six months after the patient’s death and to have assessed other patients not attending the hospital. Found guilty of serious professional misconduct and struck off the medical register.

Examples of cases considered

Two consultant gynaecologists, one academic and one non-academic, published articles purporting to report events that had not happened, as well as to have carried out studies known not to have been conducted, and to have reported findings known not to have occurred. Both were found guilty of serious professional misconduct: one was erased from the medical register, the other has been suspended.
Examples of cases considered

A general practitioner forged multiple patient signatures (191 forgeries) and other data in 21 studies. Found dead in swimming pool after submission of two statutory declarations to the GMC.

Another general practitioner offered a patient a bribe of £2000 when he realised he was being investigated.

Examples of cases considered

A general practitioner who regularly conducted asthma studies used ECG traces to cover multiple attendances of the patients to which they refer and to use them as if taken for other patients. Found guilty of serious professional misconduct and erased from the medical register.
The Case of Dr E

What the monitors found

What the auditors found

Dr E

Patient signatures on the study consent forms were not consistent with patient signatures elsewhere in the hospital notes.

Treatment randomisation numbers were allocated after visit 2 instead of at visit 2.

Patients were purported to have been seen on three separate Bank Holidays.

Patient visits were purported to have taken place when the investigator was on holiday but there was no evidence of recorded cover during this period.
Dr E

Echocardiogram and nuclear medicine data for all patients were provided on forms that were no longer used in their respective departments.

“Bogus” data were attributed by the investigator to another doctor who he alleged was his "research fellow" at the time, and whose qualification as a medical practitioner was never able to be verified.

Letters to GPs indicated that certain patients were not stabilised on treatment, and thus ineligible to enter the study, even though they were entered into the study and the CRFs indicated that they were stabilised.

The hospital out-patient register verified the appointments for the patients in the study for their first and fourth visits, but their attendance for visits 2 and 3 could not be so verified.

For ECG traces and X-rays either the date on which they were taken, or the patient identification, or both, had been cut off.

Drug accountability for patients who were withdrawn from the study at an earlier stage were completed in advance and then scored out when it was realised that the patients had withdrawn.
Conclusions

History has a habit of repeating itself.
Human nature being what it is, there will always be those who transgress.

Fraud and misconduct in biomedical research needs go be recognised and dealt with appropriately, wherever it occurs.

Only by doing so will we minimise the exploitation of patients and the damage that can result.