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Scientific Misconduct in Medical Research

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Meet The Editors Meeting - Brazil

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Senior Editor, JAMA

Scientific misconduct is defined as violation of the standard codes of scholarly conduct and ethical behavior in professional scientific research.

Research Misconduct

- Sample definitions:
  - Danish definition: “Intention or gross negligence leading to fabrication of the scientific message or a false credit or emphasis given to a scientist”
  - Swedish definition: “Intentional distortion of the research process by fabrication of data, text, hypothesis, or methods from another researcher's manuscript form or publication; or distortion of the research process in other ways.”

Research Misconduct

- The consequences of scientific misconduct can be damaging for both perpetrators and any individual who exposes it.
- There are obvious public health implications attached to the promotion of medical or other interventions based on dubious research findings.

Research Misconduct: Main Types

- Fabrication – making up data or results
- Falsification – manipulating research materials, equipment, or processes or changing or omitting data (e.g., photo manipulation)
- Plagiarism – the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.
  - *Self-plagiarism is a special form of plagiarism.*

Research Misconduct

In addition, **suppression**—the failure to publish significant findings due to the results being adverse to the interests of the researcher or his/her sponsor(s)—is also a form of scientific “misconduct” because it distorts the truth as well.

Research Misconduct

- Motivation to commit scientific misconduct?
  - Career pressure
  - Ease of fabrication
- There are no "scientific police" who are trained to fight scientific crimes.
- All investigations are made by experts in science but amateurs in dealing with criminals.
- It is relatively easy to cheat although difficult to know exactly how many scientists fabricate data.

Research Misconduct

- Well publicized cases illustrate the potential role that senior academics in research institutions play in concealing scientific misconduct.
  - Even after prolonged investigations, institutions may be reluctant to take action for various reasons.
    - Fear of lawsuits
    - Fear of hurting their own reputations
    - Wishful thinking that the perpetrator will not repeat
- Journals are also often reluctant to taking action despite strong and compelling evidence.

Notable individual cases - examples

The New York Times

Science

WORLD | U.S. | N.Y. / REGION | BUSINESS | TECHNOLOGY | SCIENCE | HEALTH | SPORTS | OPINION

ENVIRONMENT | SPACE & COSMOS

NOTORIOUS DARSEE CASE SHAKES ASSUMPTIONS ABOUT SCIENCE

By WILLIAM J. BROAD
Published: June 14, 1983

The Darsee Case

In 1981, Dr. John Darsee was caught falsifying data in a cardiac study at Harvard. This accidental discovery eventually resulted in his dismissal and a 10-year moratorium on Federal research funds.

- Dr. Darsee eventually publicly apologized for two of his fraudulent papers in the New England Journal of Medicine.

  > "I am deeply sorry for allowing these inaccuracies and falsehoods to be published in the (New England) Journal and apologize to the editorial board and readers."

- In all, more than 80 fraudulent papers and abstracts were retracted at the urging of investigators from Emory University in Atlanta where Dr. Darsee worked before going to the Harvard Medical School in 1979 at the age of 31.

The Darsee Case: Co-authors

- Restating what was common sense at one time, Dr. Arnold Relman, Editor of the New England Journal of Medicine at the time, stressed that co-authors should know each other's work inside and out.
- Two of Dr. Darsee's co-authors from Emory, Relman wrote, seemed to suggest in letters of retraction that they "had no responsibility at all for what happened, simply because they are honest and had no hand in the manipulation of the data."
- Relman wrote in an editorial: "I cannot agree, and neither will most other editors."
  - **"Co-authors should at least know that the experiments and measurements were carried out as described, and they ought to understand what was done and why."**

Possible Lessons from the Darsee Case

- Co-authors must be accountable.
- Unexpectedly high productivity should (perhaps) raise concerns.
- Peer review is not a reliable method for identifying fraud.
- Once fraud is suspected in one paper, other papers should be examined.

The case of Hwang Woo-suk in South Korea

- Hwang Woo-Suk was professor at Seoul National University who fabricated a series of experiments, which appeared in high-profile journals, in the field of stem cell research.
- Until November 2005, he was considered one of the pioneering experts in the field, best known for two articles published in the journal Science in 2004 and 2005 where he reported he had succeeded in creating human embryonic stem cells by cloning.
- He was called the "Pride of Korea" in South Korea.

Hwang Woo-suk in South Korea: Timeline

- In February 2004, Hwang and his team announced that they had successfully created an embryonic stem cell with the somatic cell nuclear transfer method, and published their paper in the March 12 issue of ***Science.***
- Although Hwang had already established himself as an expert in animal cloning and secured celebrity status in South Korea in the late 1990's, this new report came as a surprise because this was the first successful case in human somatic cell cloning.
- Until Hwang's claim, it was generally agreed that creating a human stem cell by cloning was nearly impossible due to the complexity of primates.

Hwang Woo-suk in South Korea: Timeline

- Hwang's team announced an even greater achievement in May 2005, reporting that they had created 11 human embryonic stem cells using 185 eggs.
- This work, published in the June 17 issue of ***Science***, was instantly hailed as a breakthrough in biotechnology because the cells were allegedly created with somatic cells from patients of different age and gender, while the stem cell of 2004 was created with eggs and somatic cells from a single female donor.
- This meant that every patient could receive custom-made treatment with no immune reactions.

Hwang Woo-suk in South Korea: Timeline

- Hwang made headlines in May 2005 when he criticized U.S. President George W. Bush's policy on embryonic stem cell research.
- ***Time*** magazine named Hwang one of its "People Who Mattered 2004", stating that Hwang "has already proved that human cloning is no longer science fiction, but a fact of life.“

Hwang Woo-suk in South Korea: Timeline

- In November 2005, Gerald Schatten, a University of Pittsburgh researcher who had worked with Hwang for two years, made the surprise announcement that he had ceased his collaboration with Hwang.
- In an interview, Schatten commented that "my decision is grounded solely on concerns regarding oocyte (egg) donations in Hwang's research reported in 2004."

Hwang Woo-suk in South Korea: Timeline

- After receiving allegations of misconduct, his University investigated.
- On December 29, 2005, the university determined that all 11 of Hwang's stem cell lines were fabricated.
- The university announced on January 10, 2006, that Hwang's 2004 and 2005 papers in ***Science*** were both fabricated.

Hwang Woo-suk in South Korea: Timeline

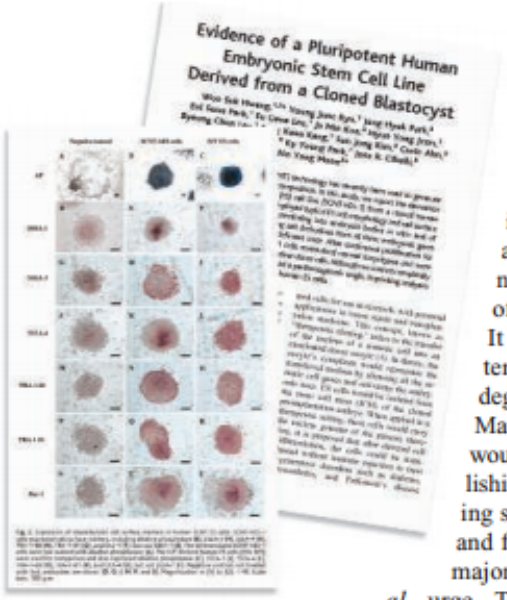
- Following on the confirmation of scientific misconduct, on January 11, ***Science*** retracted both of Hwang's papers on unconditional terms.
- On January 12, 2006, Hwang held a press conference to apologize, but still did not admit to personal misconduct.
- Instead, he explicitly put the blame on other members of his research project for having deceived him with false data and alleged a conspiracy, saying that his projects had been sabotaged and that there was theft of materials involved.

Hwang Woo-suk in South Korea: Current status

- Professor Hwang has been hired by another Korean research institute and has continued his work, including publications in credible journals.
- He was convicted in South Korea of crimes related to the source of some of his research materials (female eggs) but he never served any prison time – he was granted freedom based on governmental intervention.

Hwang Woo-suk: Reaction by *Science*

Editorial Retraction



THE FINAL REPORT FROM THE INVESTIGATION COMMITTEE of Seoul National University (SNU) (*1*) has concluded that the authors of two papers published in *Science* (*2*, *3*) have engaged in research misconduct and that the papers contain fabricated data. With regard to Hwang *et al.*, 2004 (*2*), the Investigation Committee reported that the data showing that DNA from human embryonic stem cell line NT-1 is identical to that of the donor are invalid because they are the result of fabrication, as is the evidence that NT-1 is a bona fide stem cell line. Further, the committee found that the claim in Hwang *et al.*, 2005 (*3*) that 11 patient-specific embryonic stem cells line were derived from cloned blastocysts is based on fabricated data. According to the report of the Investigation Committee, the laboratory "does not possess patient-specific stem cell lines or any scientific basis for claiming to have created one." Because the final report of the SNU investigation indicated that a significant amount of the data presented in both papers is fabricated, the editors of *Science* feel that an immediate and unconditional retraction of both papers is needed. We therefore retract these two papers and advise the scientific community that the results reported in them are deemed to be invalid.

As we post this retraction, seven of the 15 authors of Hwang *et al.*, 2004 (*2*) have agreed to retract their paper. All of the authors of Hwang *et al.*, 2005 (*3*) have agreed to retract their paper.

Science regrets the time that the peer reviewers and others spent evaluating these papers as well as the time and resources that the scientific community may have spent trying to replicate these results.

DONALD KENNEDY
Editor-in-Chief

References

1. Investigation Committee Report, Seoul National University, 10 Jan. 2006. (Members: Chairman Myung-Hee Chung, SNU, Uhtaek Oh, SNU, Hong-Hee Kim, SNU, Un Jong Pak, SNU, Yong Sung Lee, Hanyang University, In Won Lee, SNU, In Kwon Chung, Yonsei University, Jin Ho Chung, SNU)
2. W. S. Hwang *et al.*, Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst, *Science* **303**, 1669 (2004).
3. W. S. Hwang *et al.*, Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts, *Science* **308**, 1777 (2005).

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Hwang Woo-suk: Reactions by ICMJE and *Science*

- ICMJE reacted with new guidelines in 2006 that remain in place today:
  - Authorship credit should be based on:
  - 1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data;
  - 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published.

- Science adopted the same criteria beginning in 2006.

Hwang Woo-suk: Lessons?

- Similar in many ways to Darsee case
- High productivity
- Startling claims
- Poor oversight by collaborators
- Lack of accountability of collaborators

Schön scandal – Bell Labs

- Schön scandal concerns physicist Jan Hendrik Schön (born August 1970 in Verden an der Aller, Lower Saxony, Germany) who briefly rose to prominence after a series of apparent breakthroughs with semiconductors that were later discovered to be fraudulent.
- Before he was exposed, Schön had received the Otto-Klung-Weberbank Prize for Physics and the Braunschweig Prize in 2001 as well as the Outstanding Young Investigator Award of the Materials Research Society in 2002, both of which were later rescinded.
- The scandal provoked discussion in the scientific community about the degree of responsibility of coauthors and reviewers of scientific papers.
- The debate centered on whether peer review, traditionally designed to find errors and determine relevance and originality of papers, should also be required to detect deliberate fraud.

Schön scandal – Bell Labs

- In May 2002, Bell Labs set up a committee to investigate. The committee obtained information from all of Schön's coauthors and interviewed the 3 principal ones.
- The committee requested copies of the raw data but found that Schön had kept no laboratory notebooks.
- On September 25, 2002, the committee publicly released its report. The report contained details of 24 allegations of misconduct. They found evidence of Schön's scientific misconduct in at least 16 of them.
- The report found that all of the misdeeds had been performed by Schön alone.
- All of the coauthors (including the head of the team) were exonerated of scientific misconduct.
- This sparked widespread debate in the scientific community on how the blame for misconduct should be shared among co-authors, particularly when they share significant part of the credit.

Suppression and selective reporting

OPEN ACCESS

ESSAY

Why Most Published Research Findings Are False

John P. A. Ioannidis

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Summary

There is increasing concern that most current published research findings are false. The probability that a research claim is true may depend on study power and bias, the number of other studies on the same question, and, importantly, the ratio of true to no relationships among the relationships probed in each scientific field. In this framework, a research finding is less likely to be true when the studies conducted in a field are smaller; when effect sizes are smaller; when there is a greater number and lesser preselection of tested relationships; where there is greater flexibility in designs, definitions, outcomes, and analytical modes; when there is greater financial and other interest and prejudice; and when more teams are involved in a scientific field in chase of statistical significance. Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true. Moreover, for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias. In this essay, I discuss the implications of these problems for the conduct and interpretation of research.

SCIENTIFIC AMERICAN

HEALTH

An Epidemic of False Claims

Competition and conflicts of interest distort too many medical findings

By John P. A. Ioannidis on June 1, 2011

"**False positives and exaggerated results in peer-reviewed scientific studies have reached epidemic proportions in recent years.** The problem is rampant in economics, the social sciences and even the natural sciences, but it is **particularly egregious in biomedicine."**

"Many studies that claim some drug or treatment is beneficial have turned out not to be true. We need only look to conflicting findings about beta-carotene, vitamin E, hormone treatments, Vioxx and Avandia. Even when effects are genuine, their true magnitude is often smaller than originally claimed."

The Atlantic

Lies, Damned Lies, and Medical Science

Much of what medical researchers conclude in their studies is misleading, exaggerated, or flat-out wrong. So why are doctors—to a striking extent—still drawing upon misinformation in their everyday practice? Dr. John Ioannidis has spent his career challenging his peers by exposing their bad science.

"The studies were biased," he says. "Sometimes they were overtly biased. Sometimes it was difficult to see the bias, but it was there." Researchers headed into their studies wanting certain results—and, lo and behold, they were getting them. We think of the scientific process as being objective, rigorous, and even ruthless in separating out what is true from what we merely wish to be true, but in fact it's easy to manipulate results, even unintentionally or unconsciously. "At every step in the process, there is room to distort results, a way to make a stronger claim or to select what is going to be concluded," says Ioannidis.

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"There is an intellectual conflict of interest that pressures researchers to find whatever it is that is most likely to get them funded."

Perhaps only a minority of researchers were succumbing to this bias, but their distorted findings were having an outsize effect on published research. To get funding and tenured positions, and often merely to stay afloat, researchers have to get their work published in well-regarded journals, where rejection rates can climb above 90 percent. Not surprisingly, the studies that tend to make the grade are those with eye-catching findings. But while coming up with eye-catching theories is relatively easy, getting reality to bear them out is another matter. The great majority collapse under the weight of contradictory data when studied rigorously.

Medical research is not especially plagued with wrongness. Other meta-research experts have confirmed that similar issues distort research in all fields of science,

w.theatlantic.com/magazine/archive/2010/11/lies-damned-lies-and-medical-science/308269/

Dr. John Ioannidis Exposes the Bad Science of Colleagues - The Atlantic

from physics to economics (where the highly regarded economists J. Bradford DeLong and Kevin Lang once showed how a remarkably consistent paucity of strong evidence in published economics studies made it unlikely that *any* of them were right). And needless to say, things only get worse when it comes to the pop expertise that endlessly spews at us from diet, relationship, investment, and parenting gurus and pundits. But we expect more of scientists, and especially of medical scientists, given that we believe we are staking our lives on their results.

NATURE | NEWS

Social sciences suffer from severe publication bias

Survey finds that 'null results' rarely see the light of the day.

Mark Peplow

28 August 2014

- When an experiment fails to produce an interesting effect, researchers often **shelve the data and move on to another problem**.
- But withholding null results skews the literature in a field, and is a particular worry for clinical medicine and the social sciences.
- Published in Science in 2014, researchers at Stanford University measured the extent of the problem, finding that most null results in a sample of social-science studies were never published.
- This publication bias may cause others to waste time repeating the work, or conceal failed attempts to replicate published research.
- Although already recognized as a problem, "it's previously been hard to prove because unpublished results are hard to find", according to the Stanford political scientist Neil Malhotra, who led the study.

Why it's time to publish research “failures”

elsevier.com/connect/scientists-we-want-your-negative-results-too

Publishing bias favors positive results; now there's a movement to change that

By Lucy Goodchild van Hilten Posted on 5 May 2015

Publication bias: a publishing problem?

Despite their potential, negative results are repeatedly relegated to the lab books, the drawers and the trash bins. This is not a new phenomenon – research published in *Controlled Clinical Trials* in 1987 showed that statistically significant clinical trial results were three times more likely to be published than those supporting the null hypothesis.

When Matt Shipman, public information officer at North Carolina University, wrote about publishing negative results, he saw a flurry of social media activity – many researchers thought it was important, but some weren't so keen on the idea. Peter Dudek was one of the people who responded on Twitter: “If I chronicled all my negative results during my studies, the thesis would have been 20,000 pages instead of 200.”

The academic community has developed a culture that overwhelmingly supports statistically significant, “positive” results. Researchers themselves strive for these results and rush to publish them, leaving the “failed” attempts in the dust. How can this culture be shifted towards valuing negative results?

A plant science journal dedicated to negative results

It's not just the clinical trials literature that is missing negative results – any experimental discipline that works on the basis of a hypothesis runs the risk of this bias.

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Summary - Discussion