

# Why honest researchers drift to questionable research practices?

Hervé Maisonneuve, MD

[www.redactionmedicale.fr](http://www.redactionmedicale.fr)

Lyon, February 16, 2017

**Associate professor, Public health**

**President European Association of Science Editors 1996-1999**

**Chief Editor of European Science Editing 2000-2006**

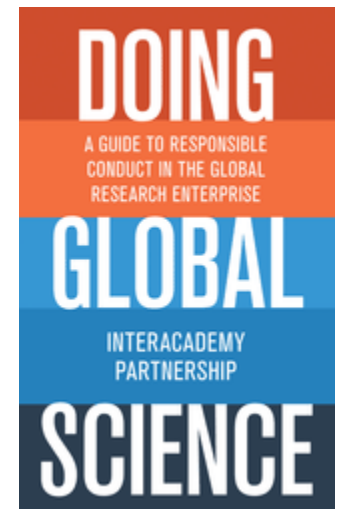
**Board JAMA 1997-2000**

# Disclosure

- Editor [www.redactionmedicale.fr](http://www.redactionmedicale.fr)
- Editor 
- Consultant: medical writing
- Member of the group on Research Integrity for the MESR
- Scientific committee of the International Institute for Research and Action on Fraud and Plagiarism in Higher Education and Research (Geneva)
- Author 'La rédaction médicale', Doin, 2010
- Editor 'Science Editors' Handbook', EASE 2013



# Corvol report on Research Integrity, June 2016



# STAP/Nature: stem cells 2014



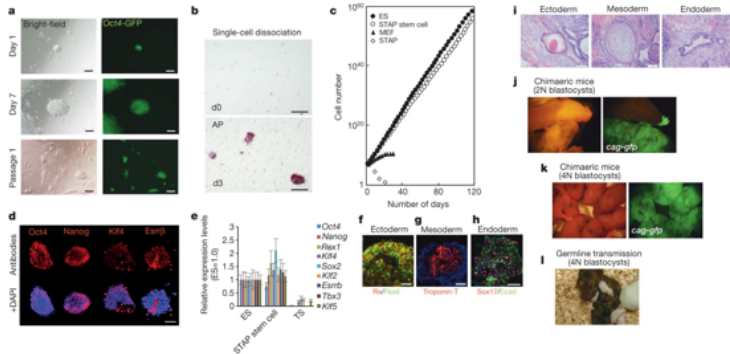
## ARTICLE

doi:10.1038/nature12968

### Stimulus-triggered fate conversion of somatic cells into pluripotency

Haruko Obokata<sup>1,2,3</sup>, Teruhiko Wakayama<sup>3†</sup>, Yoshiki Sasai<sup>4</sup>, Koji Kojima<sup>1</sup>, Martin P. Vacanti<sup>1,5</sup>, Hitoshi Niwa<sup>6</sup>, Masayuki Yamato & Charles A. Vacanti<sup>1</sup>

ES-cell-like stem cells can be derived from STAP cells.



H Obokata et al. Nature 505, 641-647 (2014) doi:10.1038/nature12968

## RETRACTION

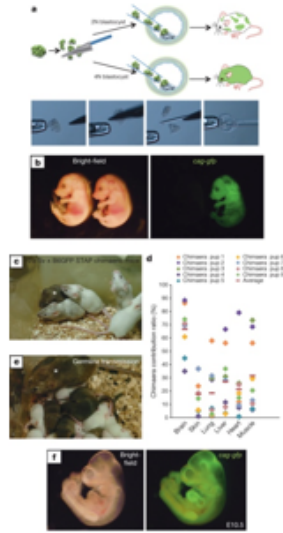
doi:10.1038/nature13598

### Retraction: Stimulus-triggered fate conversion of somatic cells into pluripotency

Haruko Obokata, Teruhiko Wakayama, Yoshiki Sasai, Koji Kojima, Martin P. Vacanti, Hitoshi Niwa, Masayuki Yamato & Charles A. Vacanti



Chimaeric mouse generation from STAP cells.



# Scientific misconduct

- **Fraud is rare (except plagiarism)**

**FFP:** Fabrication, Falsification, Plagiarism

- **Questionable Research Practices are frequent (50% of papers?)**

Grey zone between good practices and sloppy science

QRPs operate in the ambiguous space between what one might consider best practices and academic misconduct

First mention in 1958

# Pressure on researchers

- **Publish or Perish ; Publish and Perish ; Publish early and dirty**
- **Promotion and resources allocation were based on publications (impact factor) in the 80s**

**Fraud & science**  
**Small risk, high reward**

# What are the journals' goals?

- State the anteriority of scientific work
  - Dissemination of data to the scientific public
  - Validation: assess the quality of the results to be published
  - Archiving the results of science
- 
- *Facilitate the academic promotion!*
  - *Allocation of resources!*



## The STM Report

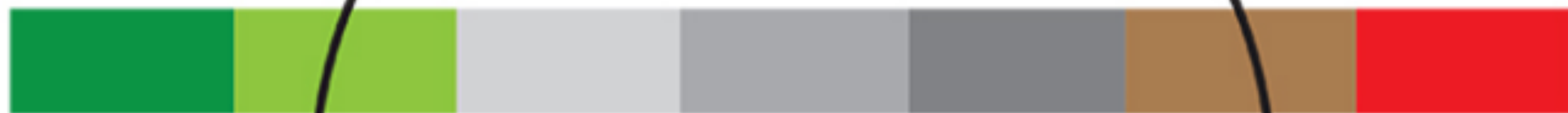
An overview of scientific and scholarly journal publishing

Celebrating the 350<sup>th</sup> anniversary of journal publishing

Good  
Research  
Practices

Questionable  
Research  
Practices

Fabrication  
Falsification  
Plagiarism



'Ideal'

Sloppy

Un-conscious bias

Conscious bias

Falsification

Fabrication





**QRPs exist in all scientific domains**

**Frequency:**

**Medicine / biology**

**Versus physics, preclinical, social sciences, etc...**

# 'Oops, Wrong Cancer': How Contaminated Cell Lines Produce Bad Research

2010;127:1-8



**Check your cultures! A list of cross-contaminated or  
misidentified cell lines**

The Atlantic 23 avril 2012

<http://www.theatlantic.com/health/archive/2012/04/oops-wrong-cancer-how-contaminated-cell-lines-produce-bad-research/256246/>

QRPs Feb 2017

# Hundreds of researchers are using the wrong cells. That's a major problem.

with 5 comments

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*What if we told you that approximately 1 in 6 researchers working with human cells are using the wrong cell line? In other words, they believe they are studying the effects of a drug on breast cancer cells, for instance, but what they really have are cells from the bladder. That is the unfortunate reality in life science research today, affecting hundreds of labs. It's a major source of problematic papers which cannot be replicated, wasting scientists' time and funding.*

*We're pleased to present a guest post from Amanda Capes-Davis, chair of the International Cell Line Authentication Committee (ICLAC), a voluntary scientific committee created to improve awareness of misidentified cell lines. She also collects news about cell line and culture contamination. This is the first in a series of two posts from guest authors about how problematic cell lines are contaminating the scientific literature, and how we can clean it up.*

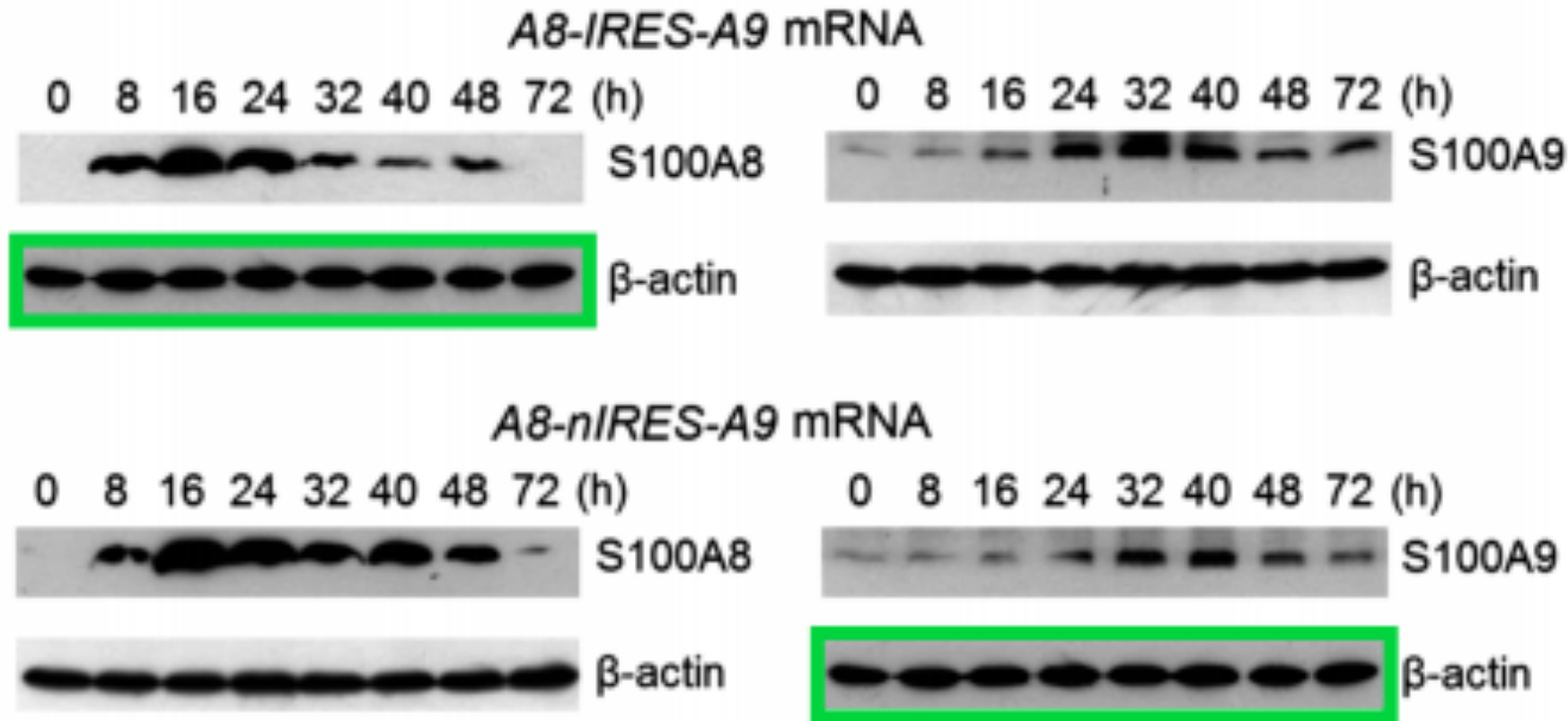
In 2010, I worked alongside Ian Freshney of Glasgow University and other colleagues to publish a list of cross-contaminated or otherwise misidentified cell lines in the International Journal of Cancer. This database of false cell lines is now curated by the International Cell Line Authentication Committee (ICLAC).



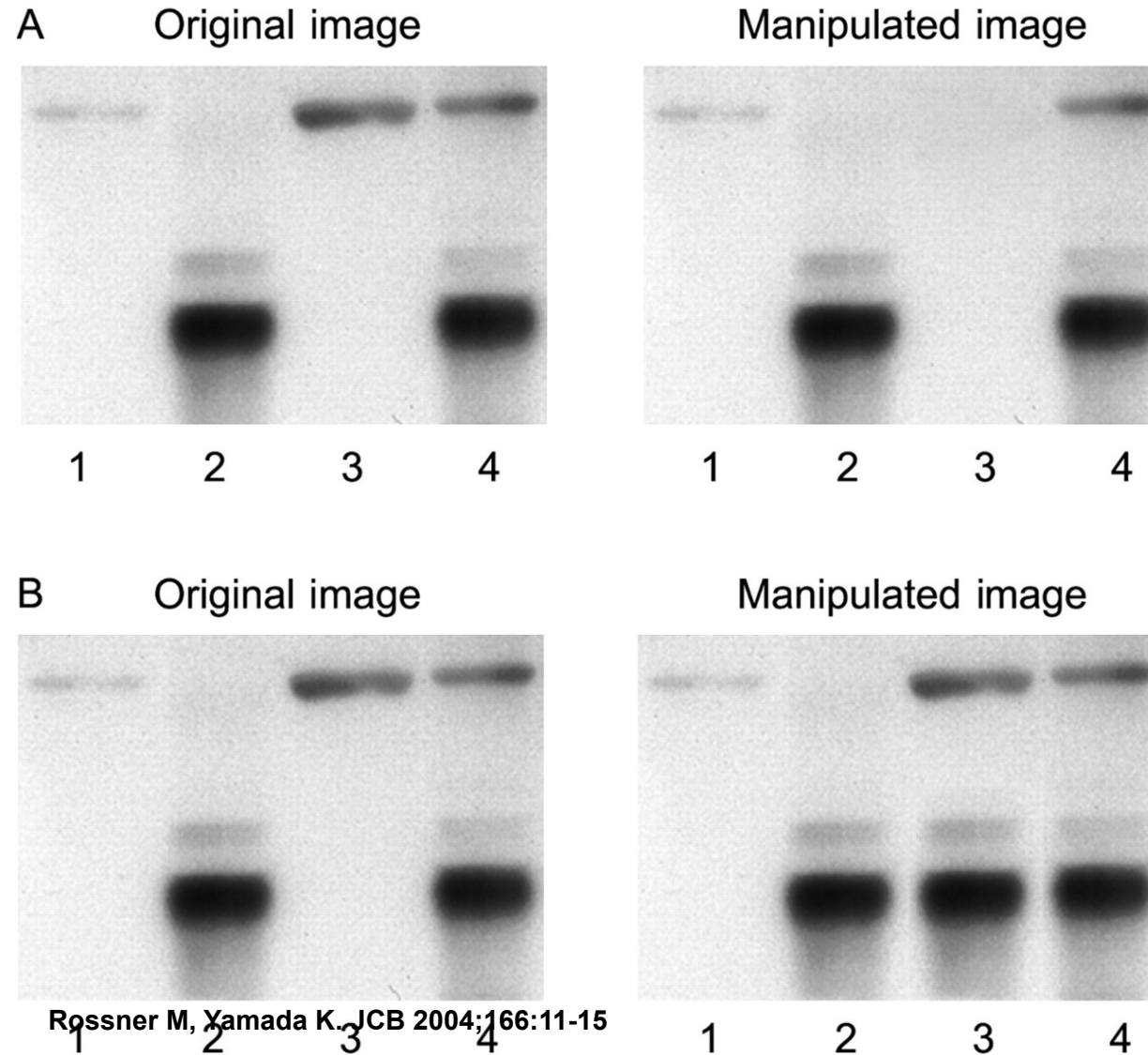
Amanda Capes-Davis

# Image duplication

The images from a total of 20,621 papers in 40 scientific journals from 1995-2014 were visually screened. Overall, 3.8% of published papers contained problematic figures, with at least half exhibiting features suggestive of deliberate manipulation.



# Gross manipulation of blots

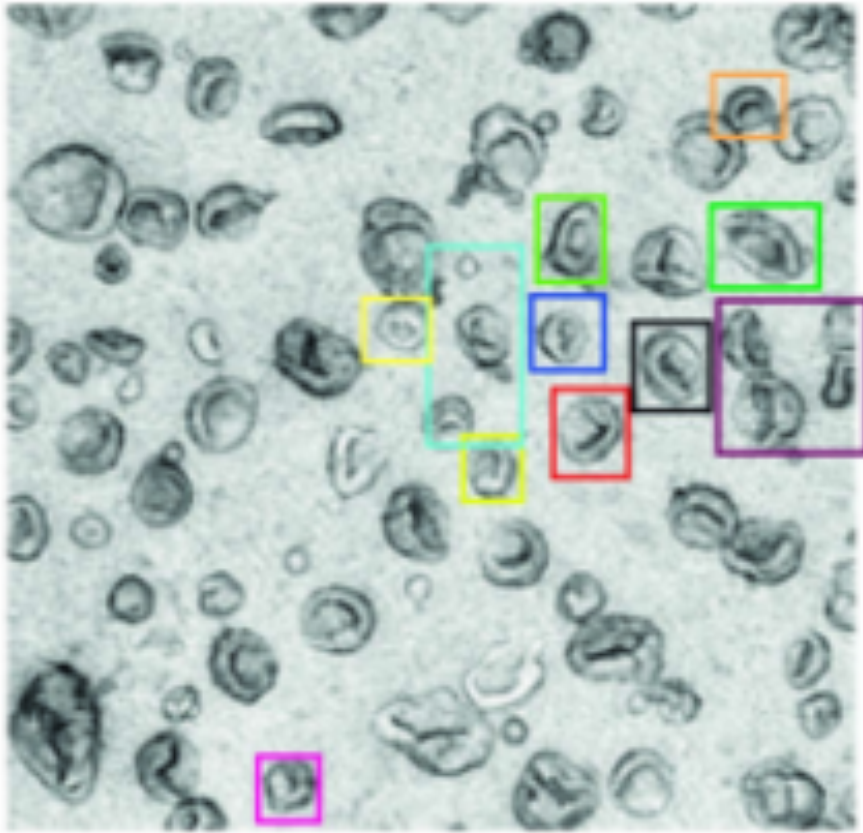




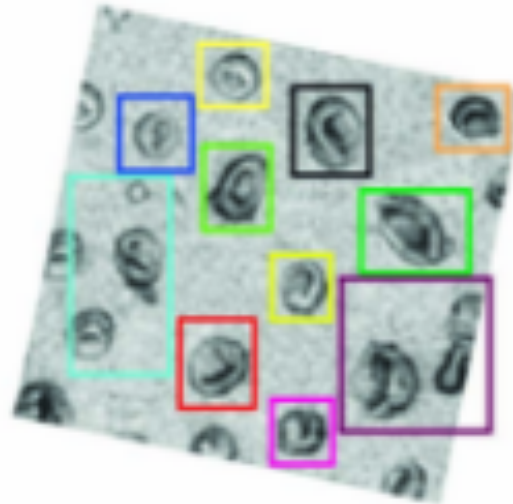
# Electronic microscopy

- PubPeer, September 2015
- Retracted by the editor in June 2016

Couzin J., Science, 2005



Li et al., Lung Cancer, 2014



## $\beta$ -Elemene against human lung cancer via up-regulation of P53 protein expression to promote the release of exosome

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### ARTICLE INFO

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**Keywords:**  
 $\beta$ -Elemene  
Lung cancer  
P53  
Exosome  
Bel-2  
Bel-x1

### ABSTRACT

**Background:**  $\beta$ -Elemene, a novel antitumor P53 derivative, isolated from the traditional Chinese medicinal herb Zedoary, has been shown to be effective against a wide variety of tumors. Recent studies have indicated that  $\beta$ -elemene can inhibit the growth of lung cancer cells; however, the exact mechanism of  $\beta$ -elemene's action in lung cancer remains largely unknown. In the present study, the antitumor effect of  $\beta$ -elemene on human lung cancer cells and the mechanism involved has been investigated.

**Methods:** The inhibitory effects of  $\beta$ -elemene on cell growth were measured by Trypan Blue exclusion and MTT assay. Flow cytometric analysis was used to detect the cell's apoptotic rate. The expression of P53 mRNA and protein were measured by RT-PCR and Western blot analysis, respectively. Exosomes were isolated by differential centrifugation and analyzed by electron microscopy and western blotting. P53 knockdown cells were established through transfection with P53 siRNA. To investigate the effect of  $\beta$ -elemene on the tumor growth, a xenograft nude mouse model was established by injecting the A549 cells into the back of nude mice.

**Results:**  $\beta$ -Elemene remarkably inhibited growth and induced apoptosis in lung cancer cells. The levels of the apoptosis-related genes Bel-2 and Bel-x1 in A549 cells decreased, while expression of P53 and production of exosomes increased after  $\beta$ -elemene treatment. Further siRNA studies suggested that the effect of  $\beta$ -elemene on tumor growth is dependent on P53 expression. Exosomes derived from A549 cultured with  $\beta$ -elemene inhibited tumor growth in nude mice. In conclusion,  $\beta$ -elemene inhibited tumor cell proliferation. The in vivo study demonstrated that  $\beta$ -elemene inhibited tumor growth and up-regulated the expression of P53 and the release of exosomes.

**Conclusion:** Our results demonstrated  $\beta$ -elemene acts on lung cancer cells in a P53 dependent manner and exosomes are involved in the regulation of cell proliferation.

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### 1. Introduction

Lung cancer continues to be the most common cause of cancer-related mortality in both men and women worldwide, killing more people than any other cancer, including breast and colon cancers combined [1]. The trend in five-year relative survival rates of lung cancer patients is only 15%. Although some therapeutic advances have been achieved, such as chemotherapy that provides useful pallia-

enhance the antitumor effects of chemotherapeutic agents are required [2]. Numerous natural cancer chemopreventive agents have already been isolated and are being used for the treatment of cancers, such as taxol and bufalin [4,5].

Elemene (1-methyl-1-vinyl-2,4-dioxopropyl-cyclohexane), an effective antitumor medicine, is isolated from the traditional Chinese medicinal herb Zedoary and contains  $\alpha$ -,  $\beta$ - and  $\delta$ -elemene.  $\beta$ -elemene, the major active antitumor component, has been shown to inhibit tumor growth and induce apoptosis in

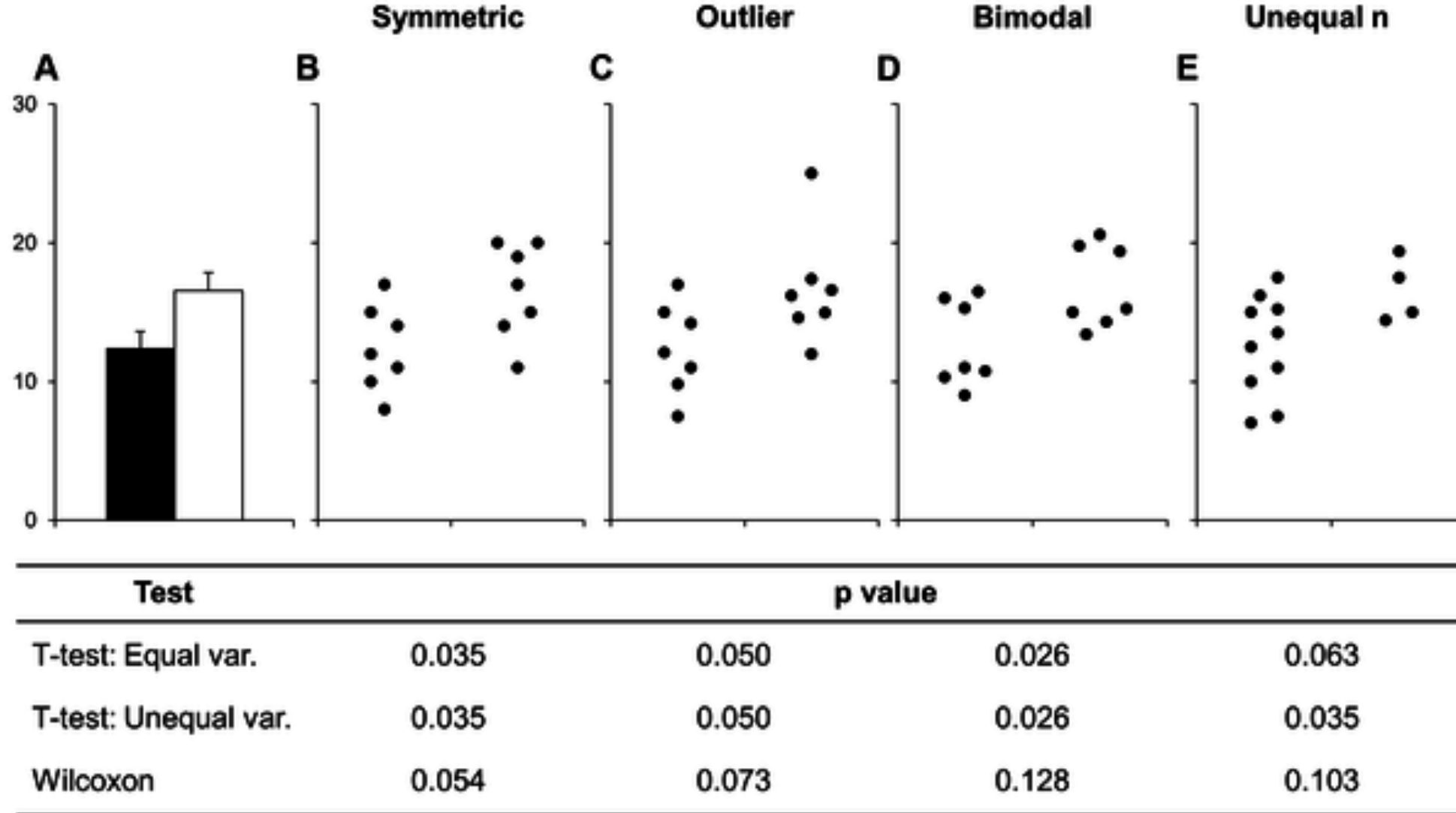
Lung Cancer. 2014 Nov;86(2):144-50. doi: 10.1016/j.lungcan.2014.08.015. Epub 2014 Aug 29.

5 comments on PubPeer

**$\beta$ -Elemene against human lung cancer via up-regulation of P53 protein expression to promote the release of exosome.**

Li J<sup>1</sup>, JunYu<sup>2</sup>, Liu A<sup>3</sup>, Wang Y<sup>4</sup>.

QRPs Feb 2017



# Analysis of 7 321 references

Out of 559 studies screened we included 28 in the main analysis, and estimated major, minor and **total quotation error rates** of 11,9%, 95% CI [8.4, 16.6] 11.5% [8.3, 15.7], and **25.4% [19.5, 32.4]**. While heterogeneity was substantial, even the lowest estimate of total quotation errors was considerable (6.7%). Indirect references accounted for less than one sixth of all quotation problems. The findings remained robust in a number of sensitivity and subgroup analyses (including risk of bias analysis) and in meta-regression.

PeerJ

✓ PEER-REVIEWED

Quotation accuracy in medical journal articles—a systematic review and meta-analysis

<https://peerj.com/articles/1364/>





# The Quarterly Journal of Experimental Psychology

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/pqje20>

## A peculiar prevalence of p values just below .05

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<sup>b</sup> Department of Health Sciences , Université du Québec à Chicoutimi , Chicoutimi , QC , Canada

Accepted author version posted online: 13 Jul 2012. Published online: 02 Aug 2012.

**2008, 12 numéros de 3 revues, 3627 p**

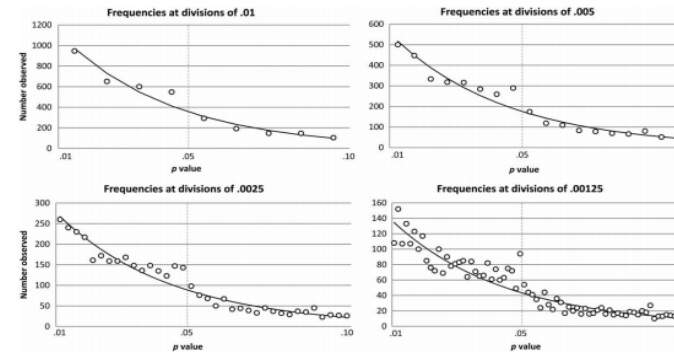
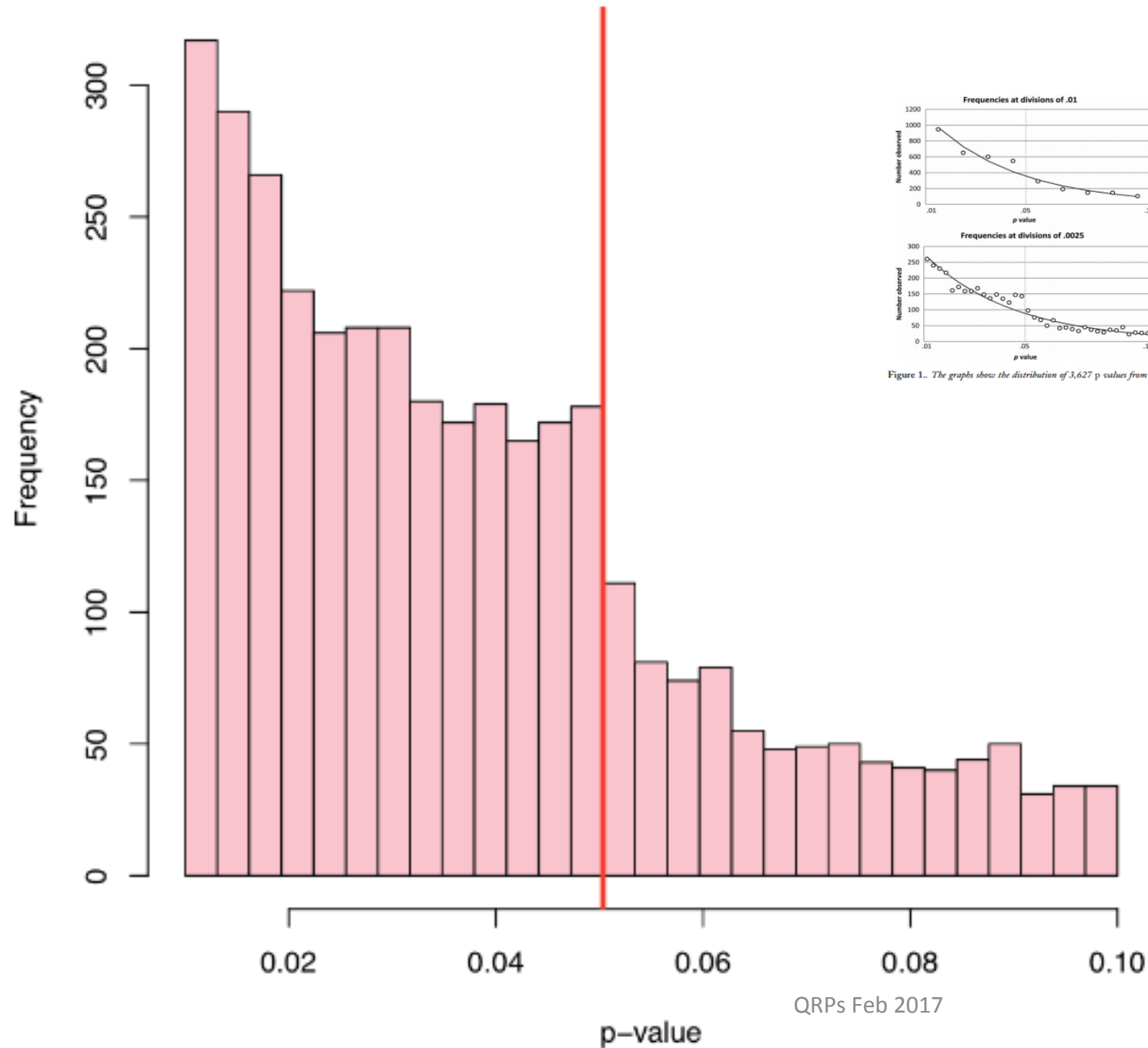


Figure 1. The graphs show the distribution of 3,627 p values from three major psychology journals.

Larry Wasserman

[https://  
normaldeviate.wordpress.com/  
2012/08/16/p-values-gone-wild-  
and-multiscale-madness/](https://normaldeviate.wordpress.com/2012/08/16/p-values-gone-wild-and-multiscale-madness/)

# Statistics

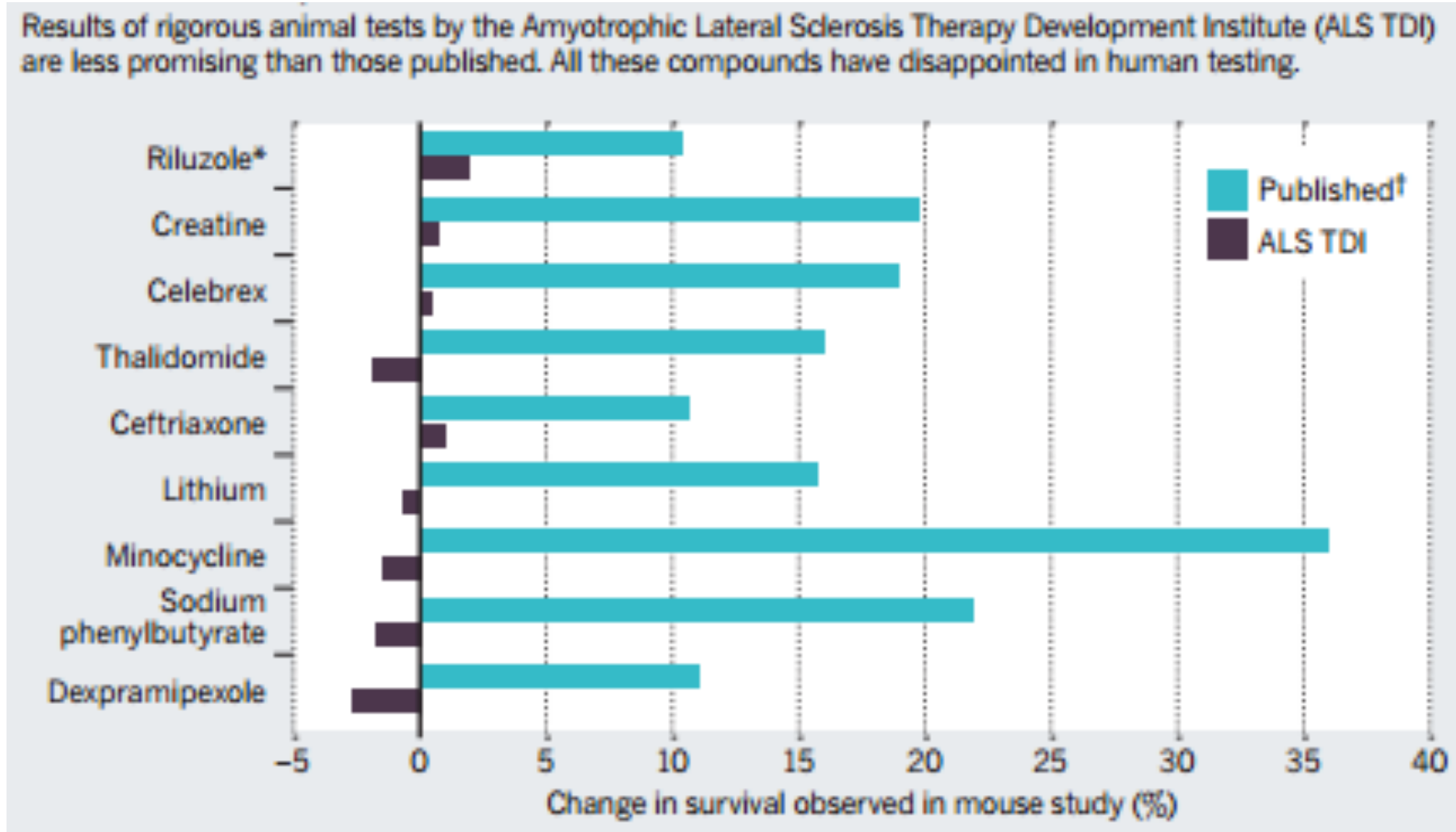
- Analysis of 250 000 P values (30 717 articles)
- 8 psychology journals
- *In line with earlier research, we found that half of all published psychology papers that use NHST\* contained at least one p-value that was inconsistent with its test statistic and degrees of freedom.*
- 12,5% major errors
- No change during time

## The prevalence of statistical reporting errors in psychology (1985–2013)

Michèle B. Nuijten<sup>1</sup> • Chris H. J. Hartgerink<sup>1</sup> • Marcel A. L. M. van Assen<sup>1</sup> • Sacha Epskamp<sup>2</sup> • Jelte M. Wicherts<sup>1</sup>


\*NHST null-hypothesis significance testing

# Preclinical research: animals

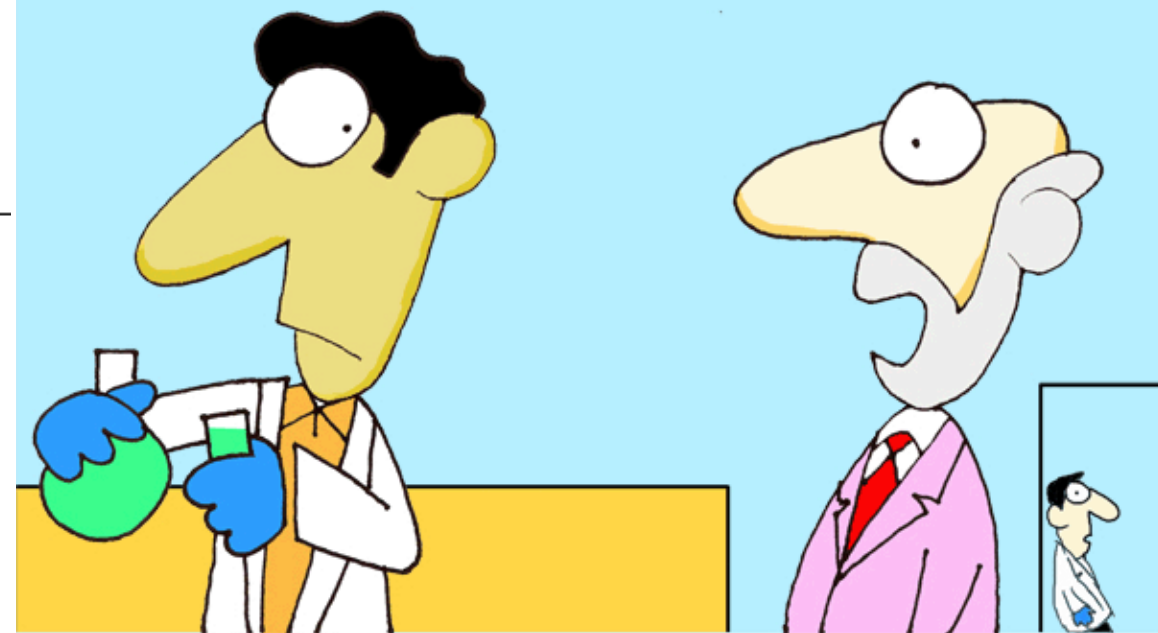


# Authors !

## Honorary and ghost authorship in high impact biomedical journals: a cross sectional survey

 OPEN ACCESS

BMJ 2011;343:d6128 doi: 10.1136/bmj.d6128



“No, it’s my wife’s turn to be the first author on **your** paper.”

### THE AUTHOR LIST: GIVING CREDIT WHERE CREDIT IS DUE

**The first author**  
Senior grad student on the project. Made the figures.

**The third author**  
First year student who actually did the experiments, performed the analysis and wrote the whole paper. Thinks being third author is “fair”.

**The second-to-last author**  
Ambitious assistant professor or post-doc who instigated the paper.

Michaels, C., Lee, E. F., Sap, P. S., Nichols, S. T., Oliveira, L., Smith, B. S.

**The second author**  
Grad student in the lab that has nothing to do with this project, but was included because he/she hung around the group meetings (usually for the food).

**The middle authors**  
Author names nobody really reads. Reserved for undergrads and technical staff.

**The last author**  
The head honcho. Hasn’t even read the paper but, hey, he got the funding, and his famous name will get the paper accepted.

www.phdcomics.com

- Honorary or gift
- Ghosts (industry & academic research)

# Criteria for authorship

**The ICMJE recommends that authorship be based on the following 4 criteria:**

**1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work;**

**AND**

**2. Drafting the work or revising it critically for important intellectual content;**

**AND**

**3. Final approval of the version to be published;**

**AND**

**4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part**

# Research Misconduct Identified by the US Food and Drug Administration

## Out of Sight, Out of Mind, Out of the Peer-Reviewed Literature

Charles Seife, MS

### Conclusion

When the FDA finds significant departures from good clinical practice, those findings are seldom reflected in the peer-reviewed literature, even when there is evidence of data fabrication or other forms of research misconduct.



**57 published clinical trials** were identified for which an FDA inspection of a trial site had found significant evidence of 1 or more of the following problems:

- falsification or submission of false information, 22 trials (39%);
- problems with adverse events reporting, 14 trials (25%);
- protocol violations, 42 trials (74%);
- inadequate or inaccurate recordkeeping, 35 trials (61%);
- failure to protect the safety of patients and/or issues with oversight or informed consent, 30 trials (53%);
- and violations not otherwise categorized, 20 trials (35%).

**Only 3 of the 78 publications (4%) mentioned the objectionable conditions or practices found during the inspection.** For 59 papers, the inspection was finished 6 months before the publication.

No corrections, retractions, expressions of concern, or other comments acknowledging the key issues identified by the inspection were subsequently published.



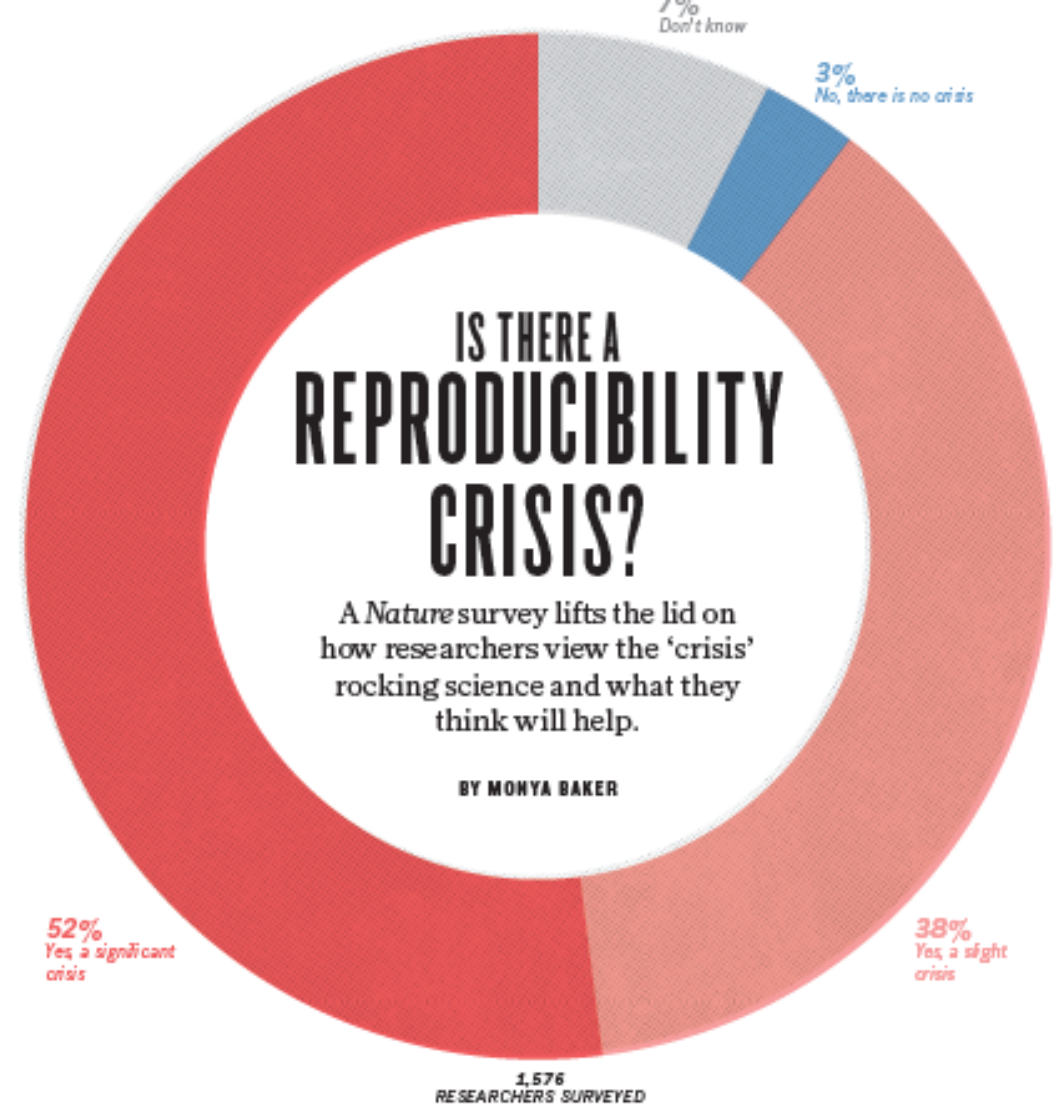
Nature, 20 May 2016

## Reproducibility

It usually means that another scientist using the same methods gets similar results and can draw the same conclusions

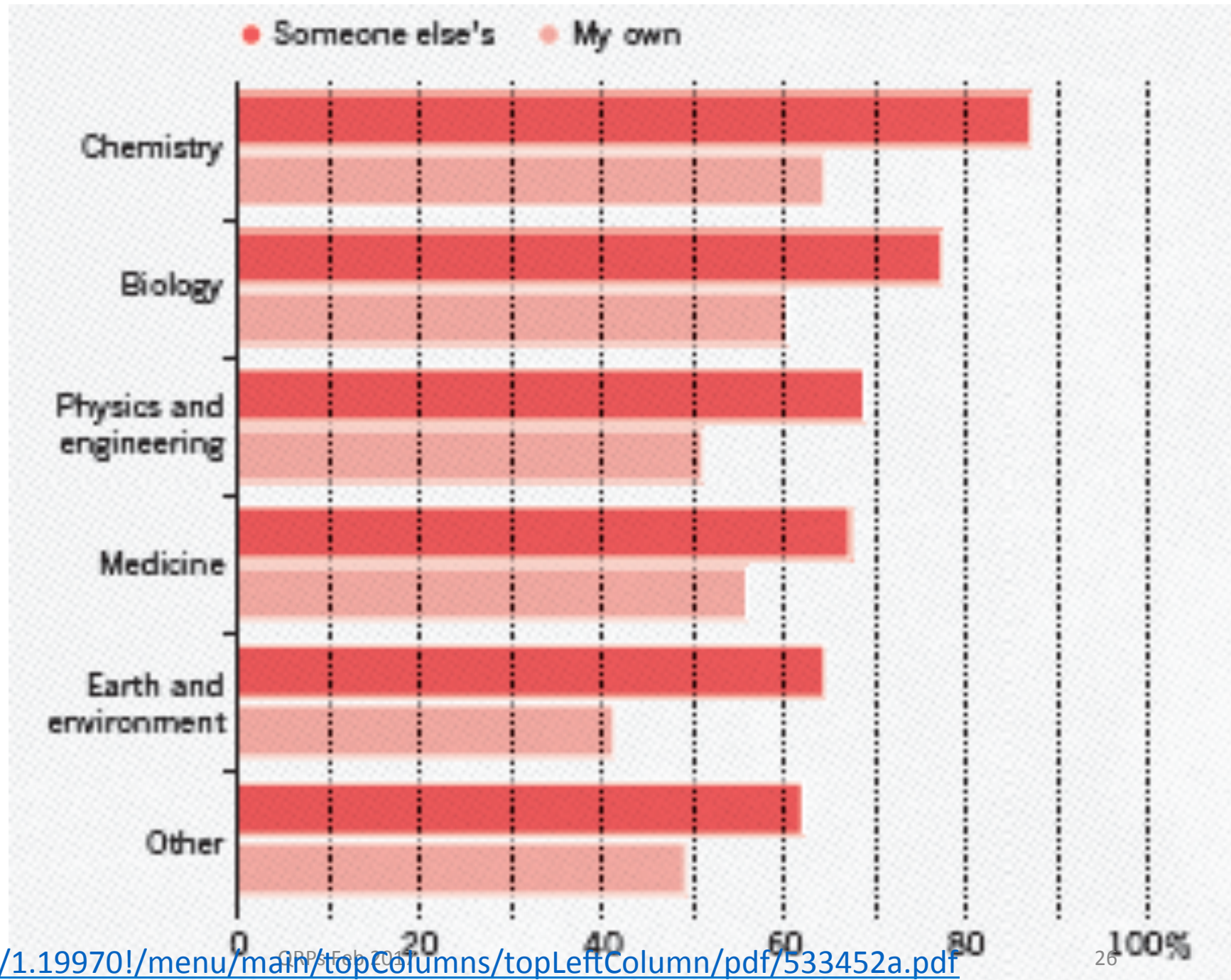
## Reality check on reproducibility

*A survey of Nature readers revealed a high level of concern about the problem of irreproducible results. Researchers, funders and journals need to work together to make research more reliable.*



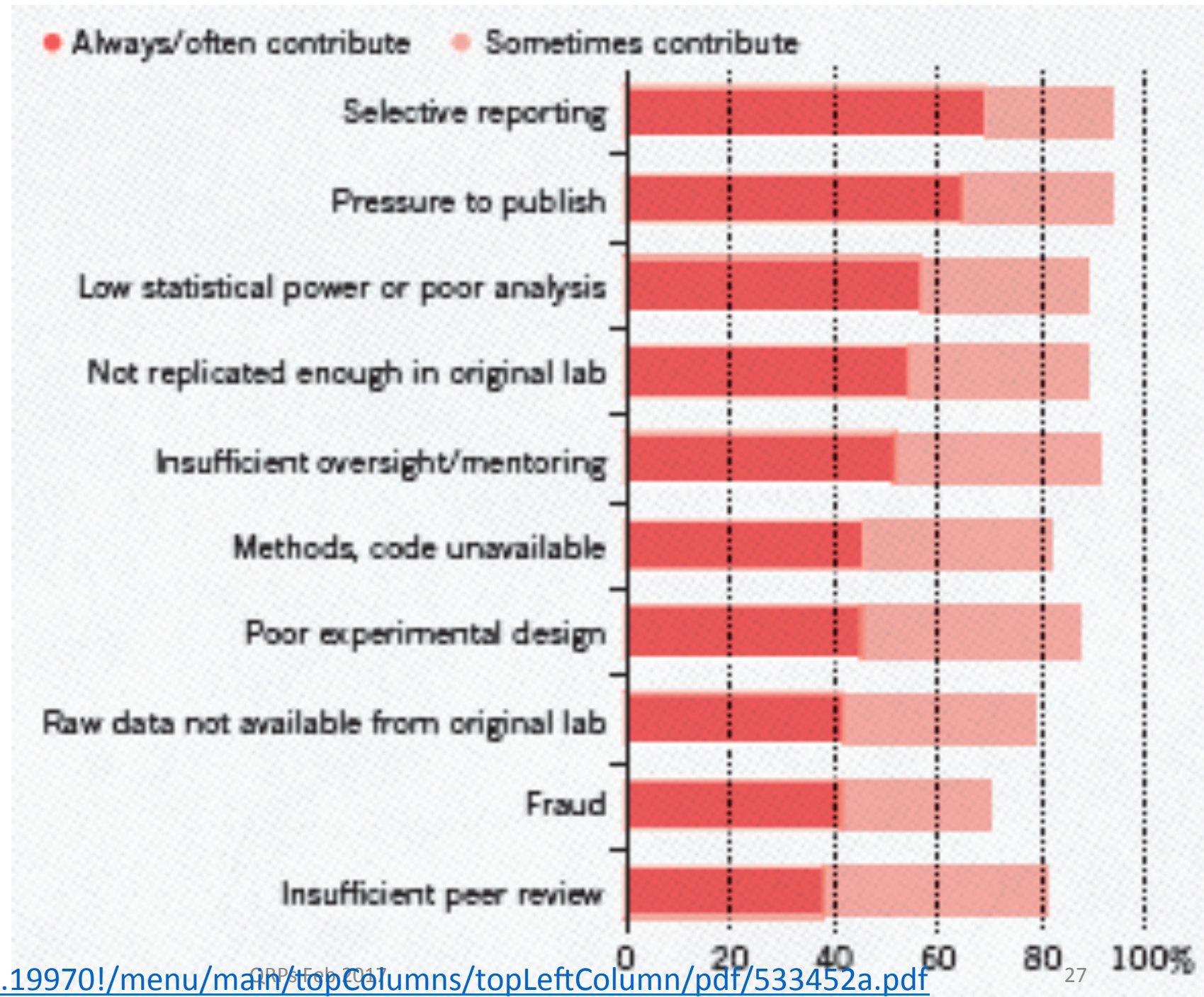
1576 answers

# Have you failed to reproduce an experiment?





# What factors contribute to irreproducible research?



## A peer-review case

You are a graduate student completing your PhD dissertation and are invited to peer-review a manuscript for a journal for the first time. The peer-review system is a hallmark of the scientific process and you are excited to be part of it. You read the abstract and believe that your expertise allows you to perform a thorough review and accept the invitation to receive the full manuscript. While reading the paper, you are able to deduce that the first author is a close personal friend with whom you worked in the past and who will soon be looking for a tenure-track position. You also notice that the paper contains significant flaws in the data-analysis section, and you believe that it should be substantially revised or rejected for that reason.

# Personal conflict of interest

**What would you do in this situation?**

**How would you disclose the conflict of interest?**

**What are the implications of not disclosing your conflict in this situation?**

## An authorship case

You are a professor who recently received tenure at one of the leading research universities in your home country after earning your PhD in another country. You are very excited about the results of recent experiments, which are significant enough to merit publication in a leading international journal. As you complete work on the manuscript for submission to one such journal, your department chair points out that acceptance of your paper will result in large financial bonuses for you and your coauthors personally and lead to a significant funding increase for the department. He suggests that you add your graduate advisor at the overseas university, who was not involved with the research but is internationally known in the field, as a coauthor of the paper....

## An authorship case

.... This would surely improve the odds that the paper will be accepted. The department chair also indicates that he expects to be a coauthor on the paper as well, even though he has not been involved with the work.

**How would you respond to the department chair?**

**What possible consequences can you foresee if you follow his suggestions?**

# 'Chrysalis' effect

## **The Chrysalis Effect: How Ugly Initial Results Metamorphosize Into Beautiful Articles**

Ernest Hugh O'Boyle, Jr., George Christopher Banks and Erik Gonzalez-Mulé

*Journal of Management* published online 19 March 2014

DOI: 10.1177/0149206314527133

1. Suggest *a posteriori* hypotheses that fit with observed data
2. Data massage to find the right answer



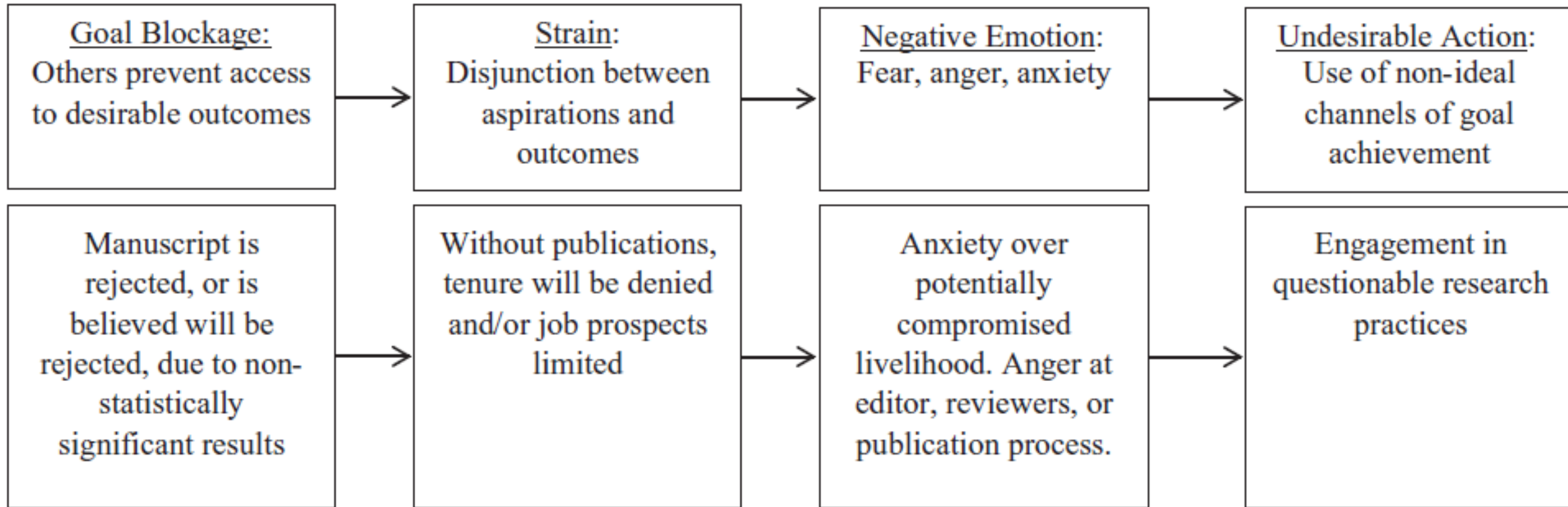
# The Chrysalis Effect: How Ugly Initial Results Metamorphosize Into Beautiful Articles

Ernest Hugh O'Boyle, Jr., George Christopher Banks and Erik Gonzalez-Mulé  
*Journal of Management* published online 19 March 2014  
DOI: 10.1177/0149206314527133

- 142 dissertation published in 83 peer-reviewed journals
- 1978 hypotheses in dissertations, & 978 in papers
- 1666 hypotheses were omitted (1333), or silently added (333) in the papers, compared with the original dissertation

*Our primary finding is that from dissertation to journal article, the ratio of supported to unsupported hypotheses more than doubled (0.82 to 1.00 versus 1.94 to 1.00). The rise in predictive accuracy resulted from the dropping of statistically nonsignificant hypotheses, the addition of statistically significant hypotheses, the reversing of predicted direction of hypotheses, and alterations to data.*

# General Strain Theory Applied to Questionable Research Practices



## Méconnaissance méthodologique

- ▶ Méthodes « faibles »
- ▶ Méthodes inappropriées
- ▶ Échantillon trop faible
- ▶ Erreurs statistiques
- ▶ Pas de recherche documentaire avant le travail
- ▶ Non-respect des réglementations

## Pratiques discutables en recherche

- ▶ « Torture » ou « massage » des données
- ▶ Changement du critère de jugement
- ▶ Choix sélectif/omission de données
- ▶ Références erronées
- ▶ Changements de tests statistiques  
*P-hacking* ou *P-HARKing*\*
- ▶ Manipulations d'images
- ▶ Paternité des articles : conflit d'auteurs !
- ▶ Études animales trompeuses
- ▶ Non-publication de recherches financées
- ▶ Résumés, communiqués de presse embellis...

## Fraude

**Fabrication**  
**Falsification**  
**Plagiat**

**Non intentionnel**

**Intentionnel**

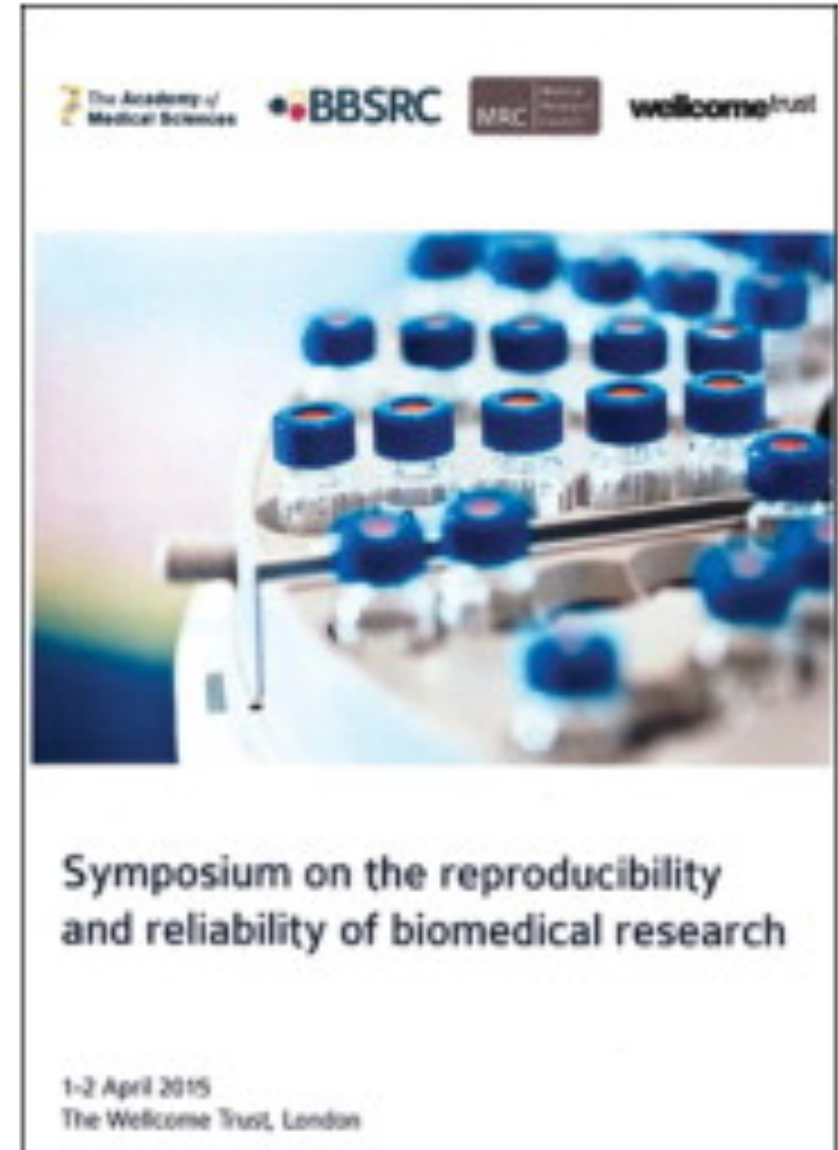
\*Hypothesizing After Results are Known

# « A lot of what is published is incorrect »

Richard Horton, Lancet editor

11 April 2015, vol 385, n° 9976, p 1380

**Change  $p < 0,05$  and adapt  $p < 0,001$**



# Quality of scientific literature?

*The case against science is straightforward: much of the scientific literature, perhaps half, may simply be untrue. Afflicted by studies with small sample sizes, tiny effects, invalid exploratory analyses, and flagrant conflicts of interest, together with an obsession for pursuing fashionable trends of dubious importance, science has taken a turn towards darkness. As one participant put it, “poor methods get results”.*

# Quality of scientific literature?

*The apparent endemicity of bad research behaviour is alarming. In their quest for telling a compelling story, scientists too often sculpt data to fit their preferred theory of the world. Or they retrofit hypotheses to fit their data. Journal editors deserve their fair share of criticism too. We aid and abet the worst behaviours. Our acquiescence to the impact factor fuels an unhealthy competition to win a place in a select few journals. Our love of “significance” pollutes the literature with many a statistical fairy-tale. We reject important confirmations. Journals are not the only miscreants.*



# Quality of scientific literature?

*Universities are in a perpetual struggle for money and talent, endpoints that foster reductive metrics, such as high-impact publication. National assessment procedures, such as the Research Excellence Framework, incentivize bad practices. And individual scientists, including their most senior leaders, do little to alter a research culture that occasionally veers close to misconduct.*

*Can bad scientific practices be fixed? Part of the problem is that no-one is incentivised to be right. Instead, scientists are incentivised to be productive and innovative.*

## Conclusion: R Horton

- *Those who have the power to act seem to think somebody else should act first.*
- *The good news is that science is beginning to take some of its worst failings very seriously.*
- *The bad news is that nobody is ready to take the first step to clean up the system.*

Lancet 2015;385:1380



# The slow science ?

## WORLD VIEW *A personal take on events*



### The pressure to publish pushes down quality

*Scientists must publish less, says Daniel Sarewitz, or good research will be swamped by the ever-increasing volume of poor work.*

- <http://www.nature.com/news/the-pressure-to-publish-pushes-down-quality-1.19887>

**Thank you**

# Au moins 50 % des articles sont embellis !

ROYAL SOCIETY  
OPEN SCIENCE

[rsos.royalsocietypublishing.org](http://rsos.royalsocietypublishing.org)



## The natural selection of bad science

Paul E. Smaldino<sup>1</sup> and Richard McElreath<sup>2</sup>

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<sup>2</sup>Department of Human Behavior, Ecology, and Culture, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany

*R. Soc. open sci.* 2016; 3: 160384.

*Peut-on croire les publications ?*  
**Biais et embellissements  
polluent la science**

*Hervé Maisonneuve*

# Declaration On Research Assessment

Sign the declaration



# DORA

## 17 recos

### For Organizations That Supply Metrics

- Be transparent
- Provide access to data
- Discourage data manipulation
- Provide different metrics for primary literature and reviews

### For Publishers

- Cease to promote journals by Impact Factor; provide an array of metrics
- Focus on article-level metrics
- Identify different author contributions
- Open the bibliographic citation data
- Encourage primary literature citations

### For Research Institutions

- When hiring and promoting, state that scientific content of a paper, not the JIF of the journal where it was published, is what matters
- Consider value from all outputs and outcomes generated by research

### For Funding Agencies

- State that scientific content of a paper, not the JIF of the journal where it was published, is what matters
- Consider value from all outputs and outcomes generated by research

### For Researchers

- Focus on content
- Cite primary literature
- Use a range of metrics to show the impact of your work
- Change the culture!