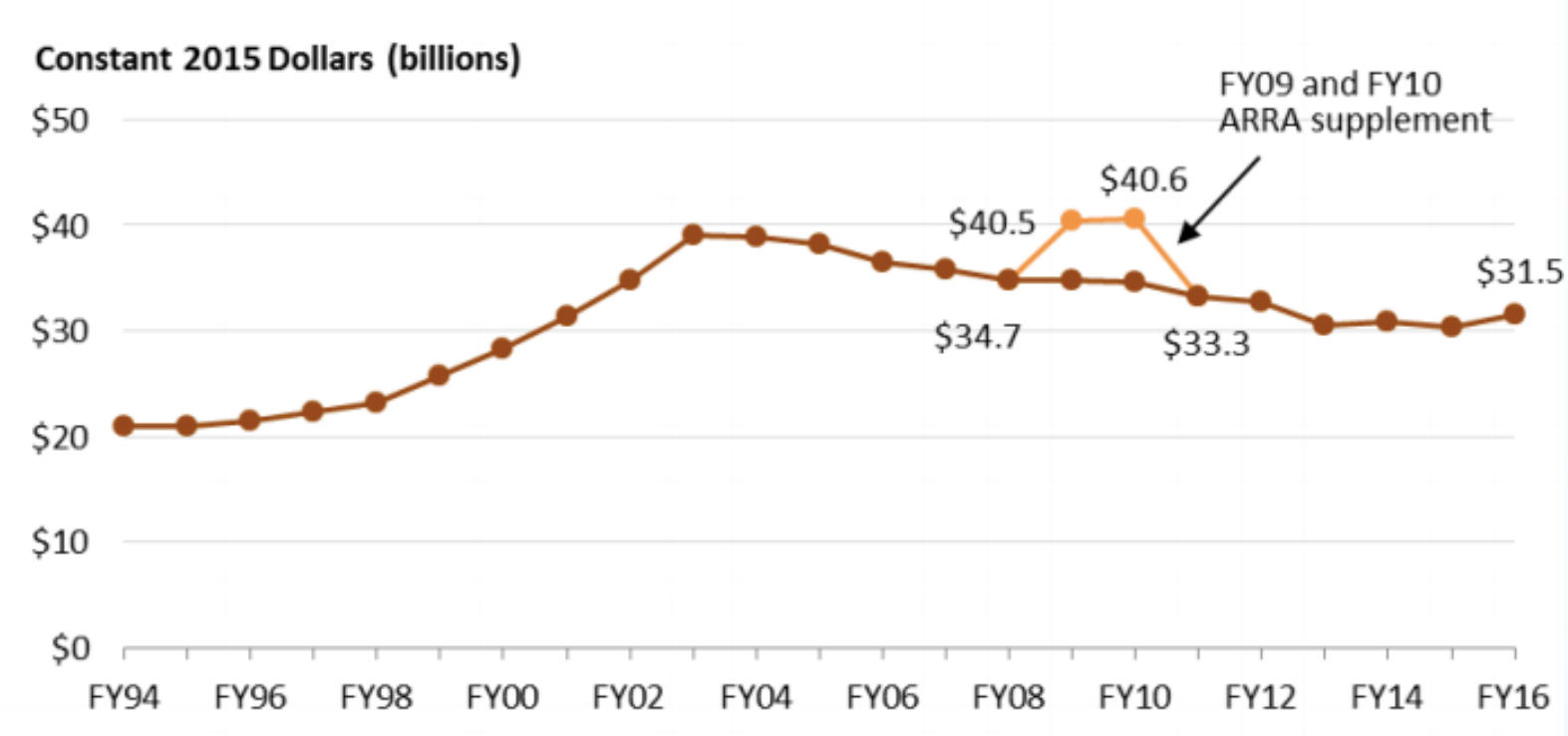
Reporting with Reproducibility in Mind

Richard Harris
NPR
13 December 2017

A Brief History



NIH Funding

Graph: Federation of American Scientists

In the long run, science is self-correcting, but “in the shorter term, the checks and balances that once ensured scientific fidelity have been hobbled.”

-Francis Collins and Lawrence Tabak

Open access, freely available online

Essay

Why Most Published Research Findings Are False

John P. A. Ioannidis

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.

factors that influence this problem and some corollaries thereof.

Modeling the Framework for False Positive Findings

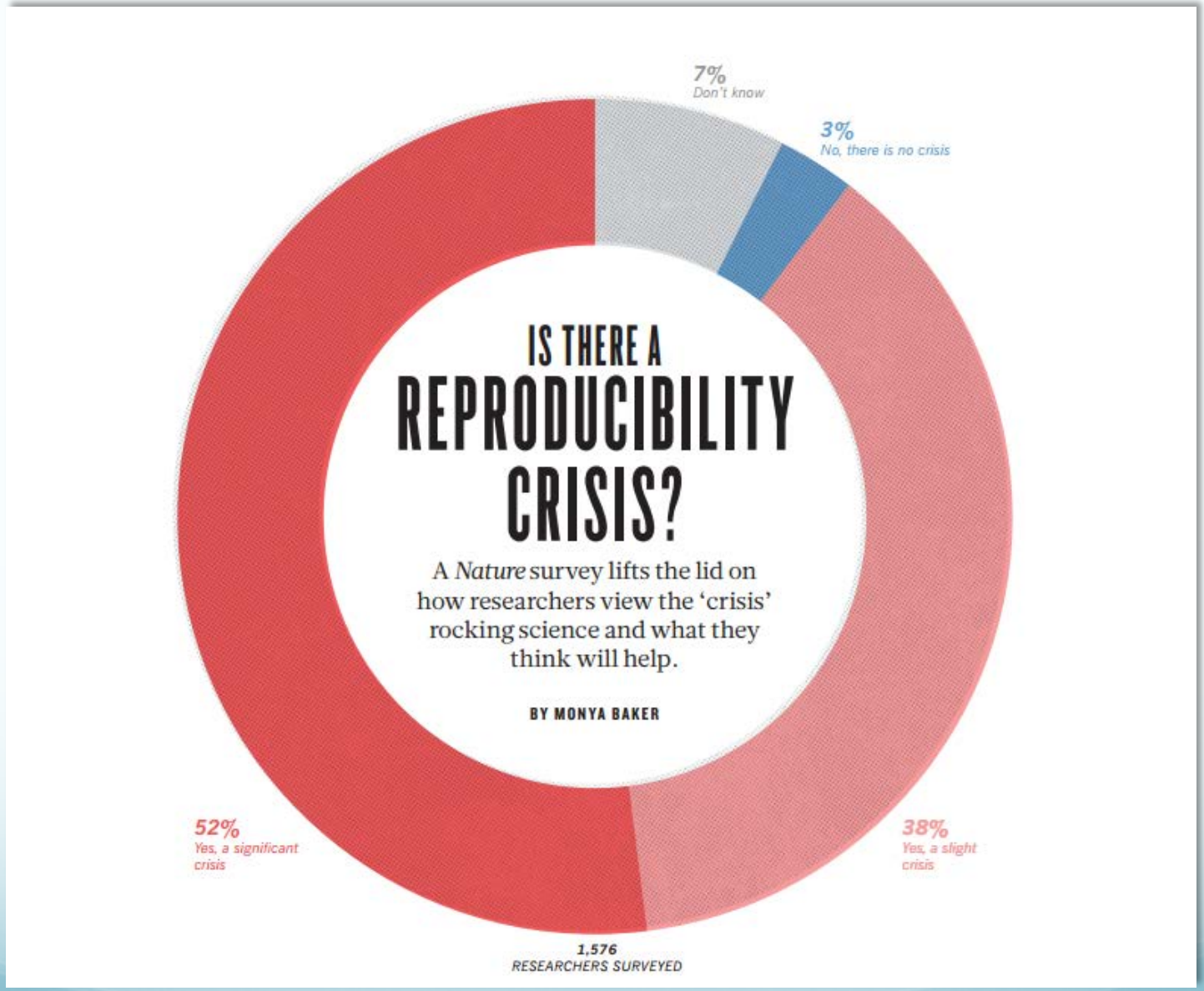
Several methodologists have pointed out [9–11] that the high rate of nonreplication (lack of confirmation) of research discoveries is a consequence of the convenient, yet ill-founded strategy of claiming conclusive research findings solely on the basis of a single study assessed by formal statistical significance, typically for a *p*-value less than 0.05. Research is not most appropriately represented and summarized by *p*-values, but, unfortunately, there is a widespread notion that medical research articles

It can be proven that most claimed research findings are false.

should be interpreted based only on *p*-values. Research findings are defined here as any relationship reaching formal statistical significance, e.g., effective interventions, informative predictors, risk factors, or associations. "Negative" research is also very useful.

is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships or searches for only one or a few true relationships among thousands and millions of hypotheses that may be postulated. Let us also consider, for computational simplicity, circumscribed fields where either there is only one true relationship (among many that can be hypothesized) or the power is similar to find any of the several existing true relationships. The pre-study probability of a relationship being true is $R/(R+1)$. The probability of a study finding a true relationship reflects the power $1 - \beta$ (one minus the Type II error rate). The probability of claiming a relationship when none truly exists reflects the Type I error rate, α. Assuming that c relationships are being probed in the field, the expected values of the 2×2 table are given in Table 1. After a research finding has been claimed based on achieving formal statistical significance, the post-study probability that it is true is the positive predictive value, PPV. The PPV is also the complementary probability of what Wacholder et al. have called the false positive report probability [10]. According to the 2

PLOS Medicine, 30 August 2005



Nature, 26 May 2016

Journalists Judging Science

Journalists Judging Science

- Is it surprising?

A Bacterium That Can Grow by Using Arsenic Instead of Phosphorus

Felisa Wolfe-Simon,[1,2]* Jodi Switzer Blum,[2] Thomas R. Kulp,[2] Gwyneth W. Gordon,[3] Shelley E. Hoeft,[2] Jennifer Pett-Ridge,[4] John F. Stolz,[5] Samuel M. Webb,[6] Peter K. Weber,[4] Paul C. W. Davies,[1,7] Ariel D. Anbar,[1,3,8] Ronald S. Oremland[2]

Life is mostly composed of the elements carbon, hydrogen, nitrogen, oxygen, sulfur, and phosphorus. Although these six elements make up nucleic acids, proteins, and lipids and thus the bulk of living matter, it is theoretically possible that some other elements in the periodic table could serve the same functions. Here, we describe a bacterium, strain GFAJ-1 of the Halomonadaceae, isolated from Mono Lake, California, that is able to substitute arsenic for phosphorus to sustain its growth. Our data show evidence for arsenate in macromolecules that normally contain phosphate, most notably nucleic acids and proteins. Exchange of one of the major bio-elements may have profound evolutionary and geochemical importance.

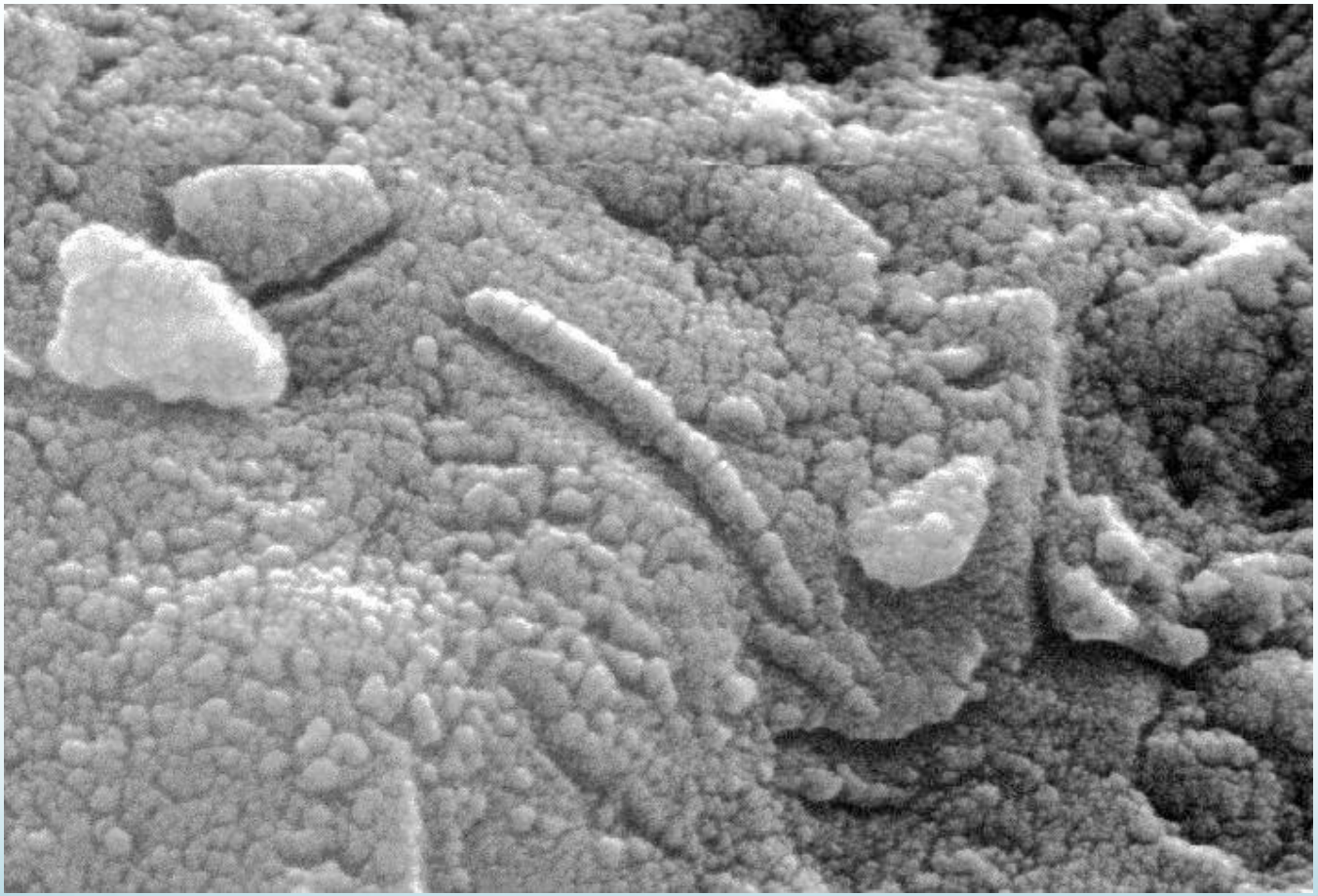
stream biochemical pathways may require the more chemically stable P-based metabolites; the lifetimes of more easily hydrolyzed As-bearing analogs are thought to be too short. However, given the similarities of As and P—and by analogy with trace element substitutions—we hypothesized that AsO_4^{3-} could specifically substitute for PO_4^{3-} in an organism possessing mechanisms to cope with the inherent instability of AsO_4^{3-} compounds (*6*). Here, we experimentally tested this hypothesis by using AsO_4^{3-}, combined with no added PO_4^{3-}, to select for and isolate a microbe capable of accomplishing this substitution.

Geomicrobiology of GFAJ-1. Mono Lake, located in eastern California, is a hypersaline and alkaline water body with high dissolved arsenic concentrations [200 μM on average (*9*)]. We used lake sediments as inocula into an aerobic defined artificial medium at pH 9.8 (*10*, *11*) containing 10 mM glucose, vitamins, and trace metals but no added PO_4^{3-} or any additional complex organic

Science 3 June 2011

Journalists Judging Science

- Is it surprising?
- Is there conflict?



NASA ALH84001

Journalists Judging Science

- Is it surprising?
- Is there conflict?
- Is it just a pitch?

EMBARGOED FOR RELEASE: 11-DEC-2017 14:00 ET (11-DEC-2017 19:00 GMT/UTC)

Scientists discover new way to help nerve regeneration in spinal cord injury

UNIVERSITY OF BRISTOL

There is currently no cure for spinal cord injury or treatment to help nerve regeneration so therapies offering intervention are limited. People with severe spinal cord injuries can remain paralysed for life and this is often accompanied by incontinence.

A team led by Drs Liang-Fong Wong and Nicolas Granger from Bristol's Faculty of Health Sciences has successfully transplanted genetically modified cells that secrete a treatment molecule shown to be effective at removing the scar following spinal cord damage. The scar in the damaged spinal cord typically limits recovery by blocking nerve regrowth.

Previous work by the team proved olfactory ensheathing cells - which are taken from the 'smell system' where they regenerate and repair throughout life to maintain sense of smell, could be genetically modified to secrete a treatment enzyme known as chondroitinase ABC (ChABC). This treatment enzyme is key in breaking down the glial scar at the injury point of the spinal cord and helping to promote nerve regrowth.

However, while previous studies have shown ChABC to be effective at promoting nerve regrowth when injected in experimental models of spinal cord injury as a drug treatment, it degrades rapidly at body temperature and repeated administration may be required to maintain efficacy.

In this study, researchers combined both treatments to treat rodents with spinal cord injury

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Journalists Judging Science

- Is it surprising?
- Is there conflict?
- Is it just a pitch?
- Is it credible?

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

Poor replication validity of biomedical association studies reported by newspapers

Estelle Dumas-Mallet, Andy Smith, Thomas Boraud, François Gonon

Published: February 21, 2017 • https://doi.org/10.1371/journal.pone.0172650

PLOS One, 21 February 2017

Replication validity of primary studies reported by newspapers

Overall, among the 156 primary studies echoed by newspapers 76 (48.7%) reported a main finding consistent with the corresponding meta-analysis (raw data are given in Supporting Information: S2 Text). Among the 156 primary studies covered by newspapers 53 were initial studies of which only 18 (34.0%) were confirmed by the corresponding meta-analyses. In contrast, of the 103 subsequent studies 58 (56.3%) were confirmed and this difference is statistically significant (Chi2 test: $X^2 = 6.99$ $p = 0.0082$). Regarding the 63 lifestyle studies

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Lessons from the Past

Lessons from the Past

- Phlogiston

JJ Becher – father of phlogiston

Source: wikipedia public domain

Lessons from the Past

- Phlogiston
- Cold Fusion

J. Electroanal. Chem., 261 (1989) 301–308
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands

Preliminary note

Electrochemically induced nuclear fusion of deuterium

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Stanley Pons *

Department of Chemistry, University of Utah, Salt Lake City, UT 84112 (U.S.A.)

(Received 13 March 1989; in revised form 22 March 1989)

INTRODUCTION

The strange behaviour of electrogenerated hydrogen dissolved in palladium has been studied for well over 100 years, and latterly these studies have been extended to deuterium and tritium [1]. For discharge of deuterium from alkaline solutions of heavy water we have to consider the reaction steps

$$D_2O + e^- \rightarrow D_{ads} + OD^- \quad \text{(i)}$$

$$D_{ads} + D_2O + e^- \rightarrow D_2 + OD^- \quad \text{(ii)}$$

$$D_{ads} \rightarrow D_{lattice} \quad \text{(iii)}$$

$$D_{ads} + D_{ads} \rightarrow D_2 \quad \text{(iv)}$$

It is known that at potentials negative to +50 mV on the reversible hydrogen scale, the lattice is in the β-phase, hydrogen is in the form of protons (as shown by the migration in an electric field) and is highly mobile ($D = 10^{-7}$ cm^2 s^{-1} for the α-phase at 300 K).

Lessons from the Past

- Phlogiston
- Cold Fusion
- Superluminal Neutrinos

nature International weekly journal of science

comments on this story

Stories by subject
- Physics

Stories by keywords
- Neutrinos
- OPERA
- MINOS
- Superluminal particles
- Special relativity
- Einstein
- Speed of light

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Add to Twitter

Published online 22 September 2011 | Nature | doi:10.1038/news.2011.554
Updated online: 23 September 2011

News

Particles break light-speed limit

Neutrino results challenge cornerstone of modern physics.

Geoff Brumfiel

An Italian experiment has unveiled evidence that fundamental particles known as neutrinos can travel faster than light. Other researchers are cautious about the result, but if it stands further scrutiny, the finding would overturn the most fundamental rule of modern physics — that nothing travels faster than 299,792,458 metres per second.

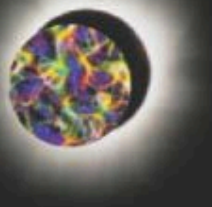
Has OPERA found super-speedy neutrinos? *CERN*

The experiment is called OPERA (Oscillation Project with Emulsion-tRacking Apparatus), and lies 1,400 metres underground in the Gran Sasso National Laboratory in Italy. It is designed to study a beam of neutrinos coming from CERN, Europe's premier high-energy physics laboratory located 730 kilometres away near Geneva, Switzerland. Neutrinos are fundamental particles that are electrically neutral, rarely interact with other matter, and have a vanishingly small mass. But they are all around us — the Sun produces so many neutrinos as a by-product of nuclear reactions that many billions pass through your eye every second.

Lessons from the Past

- Phlogiston
- Cold Fusion
- Superluminal Neutrinos
- String Theory

NOT EVEN WRONG



THE FAILURE OF STRING THEORY AND
THE SEARCH FOR UNITY IN PHYSICAL LAW

PETER WOIT

Trustworthy Science

Trustworthy Science

- Higgs Boson

Trustworthy Science

- Higgs Boson
- Climate Change

Trustworthy Science

- Higgs Boson
- Climate Change
- LIGO

ELSEVIER

Journal of Clinical Epidemiology 63 (2010) 1205–1215

Journal of Clinical Epidemiology

ORIGINAL ARTICLES

Science mapping analysis characterizes 235 biases in biomedical research

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[b]*Institut des Systèmes Complexes de Paris Ile-de-France, 57–59 rue Lhomond, 75005, Paris, France*

[c]*Department of Hygiene and Epidemiology, University of Ioannina School of Medicine and Biomedical Research Institute, Foundation for Research and Technology-Hellas, Ioannina 45110, Greece*

[d]*Tufts Clinical and Translational Science Institute and Institute for Clinical Research and Health Policy Studies, Tufts Medical Center and Department of Medicine, Tufts University School of Medicine, Boston, MA 02111, USA*

Accepted 22 December 2009

thebmj

BMJ 2015;351:h6467 doi: 10.1136/bmj.h6467 (Published 14 December 2015)

RESEARCH

CHRISTMAS 2015: THE PUBLICATION GAME

Use of positive and negative words in scientific PubMed abstracts between 1974 and 2014: retrospective analysis

Christiaan H Vinkers *assistant professor*[1], Joeri K Tijdink *psychiatrist*[2], Willem M Otte *assistant professor*[3 4]

[1]Department of Psychiatry, Brain Center Rudolf Magnus, University Medical Center Utrecht, 3584 CX Utrecht, Netherlands; [2]Department of Internal Medicine, VU University Medical Center, Amsterdam, Netherlands; [3]Department of Child Neurology, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht; [4]Biomedical MR Imaging and Spectroscopy, Center for Image Sciences, University Medical Center Utrecht, Utrecht

Results The absolute frequency of positive words increased from 2.0% (1974-80) to 17.5% (2014), a relative increase of 880% over four decades. All 25 individual positive words contributed to the increase, particularly the words "robust," "novel," "innovative," and "unprecedented," which increased in relative frequency up to 15 000%. Comparable but

Personality and Social Psychology Review
1998, Vol. 2, No. 3, 196–217

HARKing: Hypothesizing After the Results are Known

Norbert L. Kerr
Department of Psychology
Michigan State University

This article considers a practice in scientific communication termed HARKing (Hypothesizing After the Results are Known). HARKing is defined as presenting a post hoc hypothesis (i.e., one based on or informed by one's results) in one's research report as if it were, in fact, an a priori hypotheses. Several forms of HARKing are identified and survey data are presented that suggests that at least some forms of HARKing are widely practiced and widely seen as inappropriate. I identify several reasons why scientists might HARK. Then I discuss several reasons why scientists ought not to HARK. It is conceded that the question of whether HARKing's costs exceed its benefits is a complex one that ought to be addressed through research, open discussion, and debate. To help stimulate such discussion (and for those such as myself who suspect that HARKing's costs do exceed its benefits), I conclude the article with some suggestions for deterring HARKing.

nature International weekly journal of science

NATURE | NEWS

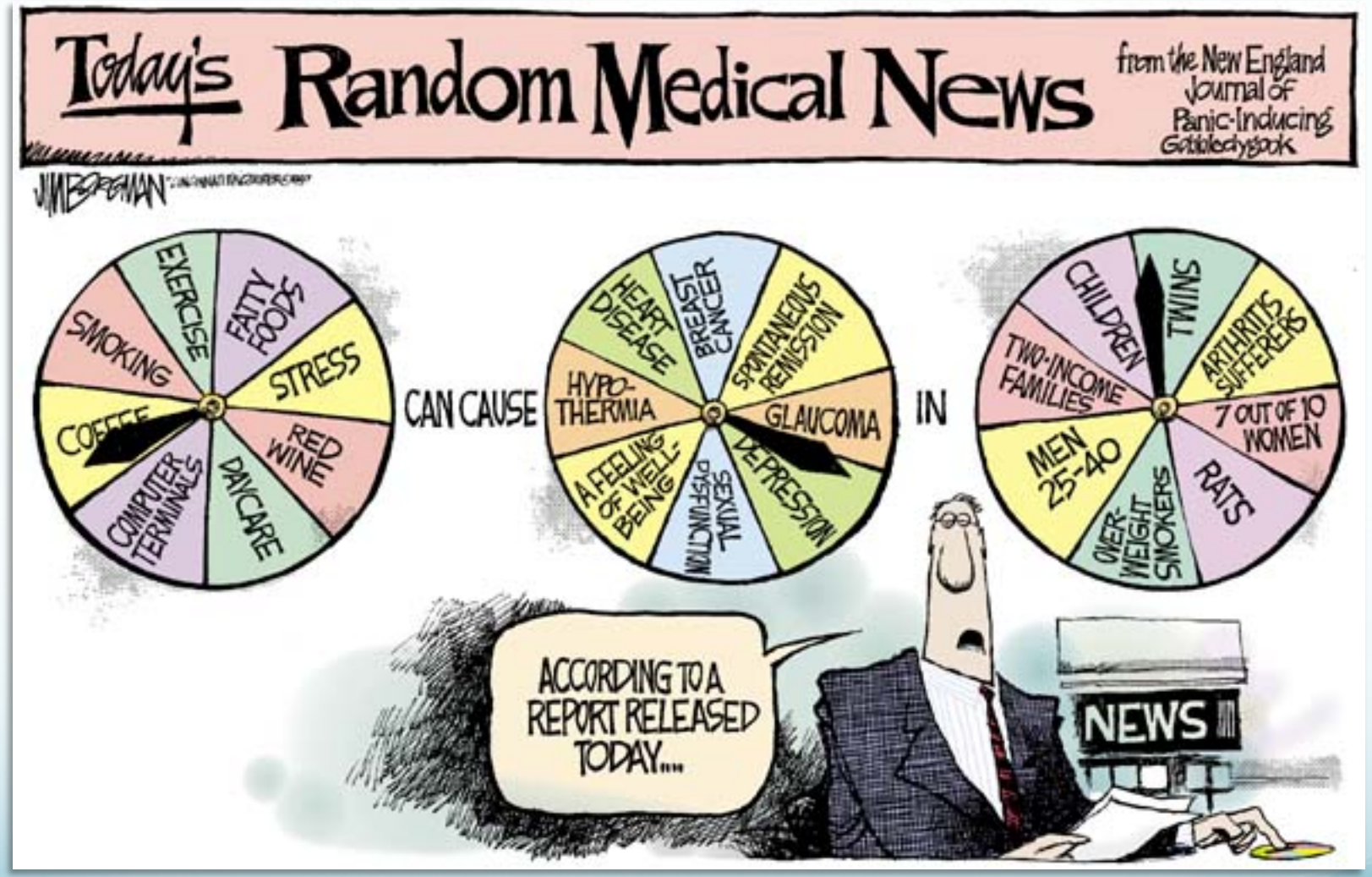
CRISPR studies muddy results of older gene research

Scientists face tough decisions when the latest gene-editing findings don't match up with the results of other techniques.

Heidi Ledford

05 April 2017

Public Perceptions



Jim Borgman, Cincinnati Inquirer and King Features Syndicate 1997

Biological Psychiatry

Archival Report

No Evidence That Schizophrenia Candidate Genes Are More Associated With Schizophrenia Than Noncandidate Genes

Emma C. Johnson, Richard Border, Whitney E. Melroy-Greif, Christiaan A. de Leeuw, Marissa A. Ehringer, and Matthew C. Keller

ABSTRACT

BACKGROUND: A recent analysis of 25 historical candidate gene polymorphisms for schizophrenia in the largest genome-wide association study conducted to date suggested that these commonly studied variants were no more associated with the disorder than would be expected by chance. However, the same study identified other variants within those candidate genes that demonstrated genome-wide significant associations with schizophrenia. As such, it is possible that variants within historic schizophrenia candidate genes are associated with schizophrenia at levels above those expected by chance, even if the most-studied specific polymorphisms are not.

METHODS: The present study used association statistics from the largest schizophrenia genome-wide association study conducted to date as input to a gene set analysis to investigate whether variants within schizophrenia candidate genes are enriched for association with schizophrenia.

RESULTS: As a group, variants in the most-studied candidate genes were no more associated with schizophrenia than were variants in control sets of noncandidate genes. While a small subset of candidate genes did appear to be significantly associated with schizophrenia, these genes were not particularly noteworthy given the large number of more strongly associated noncandidate genes.

CONCLUSIONS: The history of schizophrenia research should serve as a cautionary tale to candidate gene investigators examining other phenotypes: our findings indicate that the most investigated candidate gene hypotheses of schizophrenia are not well supported by genome-wide association studies, and it is likely that this will be the case for other complex traits as well.

Keywords: Candidate genes, Complex traits, Gene set analysis, Genome-wide association study, GWAS, Schizophrenia, Single nucleotide polymorphism, SNP

http://dx.doi.org/10.1016/j.biopsych.2017.06.033

Biological Psychiatry, 15 November 2017

Disclosure: I wrote this book.