What is the role of journals and publishers in driving research standards?

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WCRI 2015 | Rio de Janeiro
Britain’s angry white men
How to do a nuclear deal with Iran
Investment tips from Nobel economists
Junk bonds are back
The meaning of Sachin Tendulkar

HOW SCIENCE GOES WRONG.
Why Most Published Research Findings Are False
John P. A. Ioannidis

PloS Medicine 2005
doi: 10.1371/journal.pmed.0020124

Nature 2012
doi:10.1038/483531a

NRDD 2011
doi:doi:10.1038/nrd3439-c1

Raise standards for preclinical cancer research
C. Glenn Begley and Lee M. Ellis propose how methods, publications and incentives must change if patients are to benefit.

Believe it or not: how much can we rely on published data on potential drug targets?

Florian Prinz, Thomas Schiange and Khusru Asadullah
What We Talk About
When We Talk About Reproducibility
✅ We are not talking about fraud.
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✓ We acknowledge that reasonable conclusions derived from legitimate observations can be disproved by subsequent knowledge and technology advancements.
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✓ We distinguish: replication ≠ generalization ...and we draw conclusions accordingly.

✓ We must talk about and reduce irreproducibility due to cherry picking, uncontrolled experimenter bias, poor experimental design, statistical insignificance, over-fitting of models to noisy data, faulty reagents, inappropriate data presentation, ...
What can journals do?
• Tackling the widespread and critical impact of batch effects in high-throughput data, Leek et al., NRG, Oct 2010
• How much can we rely on published data on potential drug targets? Prinz et al., NRDD, Sep 2011
• The case for open computer programs, Ince et al., Nature, Feb 2012
• Raise standards for preclinical cancer research, Begley & Ellis, Nature, Mar 2012
• Face up to false positives, MacArthur, Nature, Jul 2012
• Next-generation sequencing data interpretation: enhancing reproducibility and accessibility, Nekrutenko & Taylor, NRG, Sep 2012
• A call for transparent reporting to optimize the predictive value of preclinical research. Landis et al., Nature, Oct 2012
• Know when your numbers are significant, Vaux, Nature, Dec 2012
• Reuse of public genome-wide gene expression data, Rung & Brazma, NRG, Feb 2013
• Reproducibility: Six red flags for suspect work, Begley, Nature, May 2013

http://www.nature.com/nature/focus/reproducibility/index.html
A call for transparent reporting to optimize the predictive value of preclinical research

The US National Institute of Neurological Disorders and Stroke convened major stakeholders in June 2012 to discuss how to improve the methodological reporting of animal studies in grant applications and publications. The main workshop recommendation is that at a minimum studies should report on sample-size estimation, whether and how animals were randomized, whether investigators were blind to the treatment, and the handling of data. We recognize that achieving a meaningful improvement in the quality of reporting will require a concerted effort by investigators, reviewers, funding agencies and journal editors. Requiring better reporting of animal studies will raise awareness of the importance of rigorous study design to accelerate scientific progress.
Introspection: formal corrections

Nature and Nature Research Journals

% of Published Research Articles

Corrigenda
Retractions

WCRI | June 2015
Introspection: formal corrections

- Missing controls
- Results not sufficiently representative of experimental variability
- Data selection
- Investigator bias
- Technical replicates wrongly described as biological replicates
- Contamination of primary culture cells
- Over-fitting of models for noisy datasets, e.g., fMRI, x-ray crystallography, machine learning
- Errors and inappropriate manipulation in image presentation
- Poor data management
Underlying issues

- experimental design
- statistics literacy
- data presentation
- data management
- reagents validity
- pressure to publish
- publication bias
- replications and refutations not pursued

REMEDIES

- training
- laboratory management
- leadership & mentoring
- size of laboratories
- infrastructure
- oversight and compliance
- quality assurance
- incentives for rigor,
  professionalism and good
  laboratory leadership

WCRI 2015 | Education track
Journals can take action
CONSORT guidelines

Reporting randomized clinical trials

CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomised Trials

Kenneth F. Schulz¹*, Douglas G. Altman², David Moher³, for the CONSORT Group⁴

1 Family Health International, Research Triangle Park, North Carolina, United States of America, 2 Centre for Statistics in Medicine, University of Oxford, Wolfson College, Oxford, United Kingdom, 3 Ottawa Methods Centre, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Department of Epidemiology and Community Medicine, University of Ottawa, Ottawa, Canada
Announcement: Reducing our irreproducibility
24 April 2013

Raising standards
Nature journals’ updated editorial policies aim to improve transparency and reproducibility.

Facilitating reproducibility
Nature journals are updating editorial policies with the aim of improving transparency and reproducibility.
Editorial measures at Nature
Introduced May 2013 – focus on reporting

1. Checklist of reporting standards
2. Eliminated length limits for methods sections
   • up to 50% increase
3. Increased scrutiny of statistics
   • Statistical advisor: Terry Hyslop
   • pool of statistical consultants
4. Re-emphasized data sharing
   • stress use of repositories
   • data descriptors – Scientific Data
   • source data – aka ‘data behind graphs’

nature.com/authors/checklist.pdf
Is it working?
Impact assessment
*Under way*

• Independent study commissioned: meta-analysis of published papers

• Malcolm Macleod (University of Edinburgh), Emily Sena (University of Edinburgh/ Florey Neurosciences Institute), David Howells (Florey Neurosciences Institute) – CAMARADES

• Funded by Arnold Foundation

• Focus on reporting quality and completeness

➔ Impact assessment to be published independently

➔ Actionable outcomes to guide further actions
(a) Western blot of cell lysates of control and Rac1-siRNA-treated MTLn3 cells, blotted for Rac1 and β-actin. **A representative image is shown from 3 blots.** (b) MTLn3 cells transfected with control or Rac1 siRNA and plated on Alexa-405-conjugated gelatin overnight. Arrows point to invadopodia and sites of degradation. Scale bars, 10 μm. Representative image sets are shown from 50 image sets each for the control and Rac1 siRNA. (c) Quantification of mean degradation area per cell from b, including Rac1 inhibitor NSC23766 treatment at 100 μM. **n = 60 fields for each condition, pooled from 5 independent experiments; error bars are s.e.m. Student’s t-test was used.** **P = 0.00022, ^ P = 0.011639. Uncropped images of blots are shown in Supplementary Fig. 9.
Reporting animal experiments

*Nature Neuroscience*

Jan ‘12 (10 papers)  
Oct ‘13 – Jan ‘14 (41 papers)

“Not reported” includes cases for which the specific question was not relevant (e.g. investigator cannot be blinded to treatment)
An ongoing process...
Proposed Principles and Guidelines for Reporting Preclinical Research

The signatories represent journals that publish preclinical biological research—an area of research that encompasses both exploratory studies and more defined research.

Journals unite for reproducibility

Consensus on reporting principles aims to improve quality control in biomedical research and encourage public trust in science.

Reproducibility, rigor, transparency, and independent verification are cornerstones of the scientific method. Of course, just because a result is reproducible does not necessarily make it right, and just because it is not reproducible does not necessarily make it wrong. A transparent and rigorous approach, however, can almost always shine a light on issues of reproducibility. This light ensures that science moves forward.

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Nature journals policy on computer code

Code share

Papers in Nature journals should make computer code accessible where possible.

A theme in Nature's ongoing campaign for the replicability and reproducibility of our research papers is that key components of publications should be available to peers who wish to validate the techniques and results.

A core element of many papers is the computer code used by authors in models, simulations and data analysis. In an ideal world, this code would always be transportable and easily used by others. In such a world, our editorial policy would be to insist on sharing to allow free use, as we already do (as far as is practicable) with data and research materials. Unfortunately, such an ideal is not easy to attain owing to the amount of extra funding and effort it would require to render some major pieces of code shareable. Nevertheless, we at Nature and the Nature research journals want to encourage as much sharing as possible.

Climate modellers have made some strides in this regard. The journal Geoscientific Model Development has a good example of such a policy (see go.nature.com/jv8g1w), and an article in Nature Geoscience discusses some of the opportunities presented by code sharing, as well as the obstacles (S. M. Easterbrook Nature Geosci. 7, 779–781; 2014).

As a leading example of transparency policies in other disciplines, the data journal GigaScience requires code used in its papers to be available, and hosts it in a way that allows others to analyse the data in publications. One point made by Easterbrook is that even if the code is shared, others might often make little or no use of it, but on some occasions the take-up will be large.

Nature and the Nature journals have decided that, given the diversity of practices in the disciplines we cover, we cannot insist on sharing computer code in all cases. But we can go further than we have in the past, by at least indicating when code is available. Accordingly, our policy now mandates that when code is central to reaching a paper's conclusions, we require a statement describing whether that code is available and setting out any restrictions on accessibility. Editors will insist on availability where they consider it appropriate: any practical issues preventing code sharing will be evaluated by the editors, who reserve the right to decline a paper if important code is unavailable. Moreover, we will provide a dedicated section in articles in which any information on computer code can be placed. And we will work with individual communities to put together best-practice guidelines and possibly more-detailed rules.

For full details, see our guide for authors at go.nature.com/o5ykhe. For an archive of our content and initiatives concerning reproducibility, see http://www.nature.com/nature/focus/reproducibility.
Data presentation

*Kick the bar chart habit!*

- We now recommend plotting individual data points for $n<5$
- *Nature Methods* worked with community to make a box plot tool available

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**BoxPlotR: a web tool for generation of box plots**

To the Editor: In biomedical research, it is often necessary to compare multiple data sets with different distributions. The bar plot, or histogram, is typically used to compare data sets on the basis of simple statistical measures, usually the mean with s.d. or s.e.m. However, summary statistics alone may fail to convey underlying differences in the structure of the primary data (Fig. 1a), which may in turn lead to erroneous conclusions. The box plot, also

[http://boxplot.tyerslab.com](http://boxplot.tyerslab.com)
Educational resources by Nature journals

Statistics for biologists and data visualization

free web collection (incl. Nature Methods ‘Points of Significance’ columns)

e-book
Reporting cell line characterization

Multiple Nature journals

n = 60 papers that report the use of cell lines
Time to tackle cells’ mistaken identity

The differences between a cow and a monkey are clear. It is easy to tell a moth from a mosquito. So why are there still scientific studies that mix them up? The answer is simple: hundreds of cell lines stored and used by modern laboratories have been wrongly identified. Some pig cells are labelled as coming from a chicken.

Problems have already been identified with 5000 cell lines.

In the long term, the goal is to ensure that all cell lines worldwide are replicated by at least three labs, and that scientists should already be aware that the cell line they are using is one of the 5000 that have been flagged.

In 2013, Nature journals started to ask authors to report the source of their cell line and whether the cell line had been authenticated. Most have not done so. Out of a sample of around 60 cell-line-based papers published across several Nature journals in the past two years, almost one-quarter did not report the source. Only 10% of authors said that they had authenticated the cell line. This is especially problematic given that almost one-third said that they had used an unauthentic cell line.

A resource for cell line authentication, annotation and quality control

Mamie Yu1*, Suresh K. Selvaraj1*, May M. Y. Liang-Chu1, Sahar Aghajani2, Matthew Busse2, Jean Yuan2, Genee Lee1, Franklin Peale3, Christiaan Klijn2, Richard Bourgon2, Joshua S. Kaminker2 & Richard M. Neve1
Journals and publishers can help facilitate credit for all contributions
Publishers support community initiatives

ORCID is a non-for-profit organization supported by publishers, funders, universities, professional societies, researchers associations.

**ORCID provides persistent unique identifiers to researchers**

- Member created
- Direct via orcid.org
- Member referred

1.35M ORCID registrants
>7M works
>200 member organizations
Mutations in the gene encoding PDGF-B cause brain calcifications in humans and mice


Nature Genetics 45, 1077–1082 (2013) | doi:10.1038/ng.2723
Received 05 April 2013 | Accepted 13 July 2013 | Published online 04 August 2013
Author contributions

Project CRedit: a taxonomy of contributions

Nature journals have mandated author contribution statements since 2009, to clarify credit and accountability.

Now working with other publishers, funders and scientists to establish a standardized vocabulary of contributions.
Data journals
Credit for production and sharing of reusable data
Article-level metrics
Alternative measures of interest and impact
Role of journals

• Raise awareness
• Be a catalyst and facilitator of discussions
• Drive some changes
• Ensure full reporting, effective review and measured conclusions
• Provide opportunities for detailed and accurate credit for all contributions
• Respond quickly and thoroughly to criticisms of published papers
Role of funders

NIH actions:

- training focused on good experimental design
- test checklist for more systematic evaluation of grant applications, incl. evaluation of scientific premise
- greater transparency of data underlying published papers
- PubMed Commons for open discussion about published articles
- new biosketch format for grant applications
Role of funders

RCUK demand strong statistics for animal studies

• justify the work and set out ethical implications
• demonstrate that the experimental design is statistically robust
Universities and institutions: target issues

• Training
• Oversight and compliance with best practices
• Laboratory size & PI time for mentoring and support
• Infrastructure and support
  – data management, reagents, validation services
  – quality assurance support
• Incentives and recognition for good laboratory leadership
Thank you for listening

My thanks to colleagues:
• Philip Campbell
• All Nature journals editors for their efforts in implementing reproducibility measures
• Kalyani Narasimhan for leading in neuroscience
• Daniel Evanko for statistics resources
• Hugh Ash for impact study
• Malcolm McLeod (Edinburgh) and CAMARADES team for impact study
• Amy Brand (Digital Science) and Liz Allen (Wellcome Trust) for CRediT

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