Ethics in Biological Research

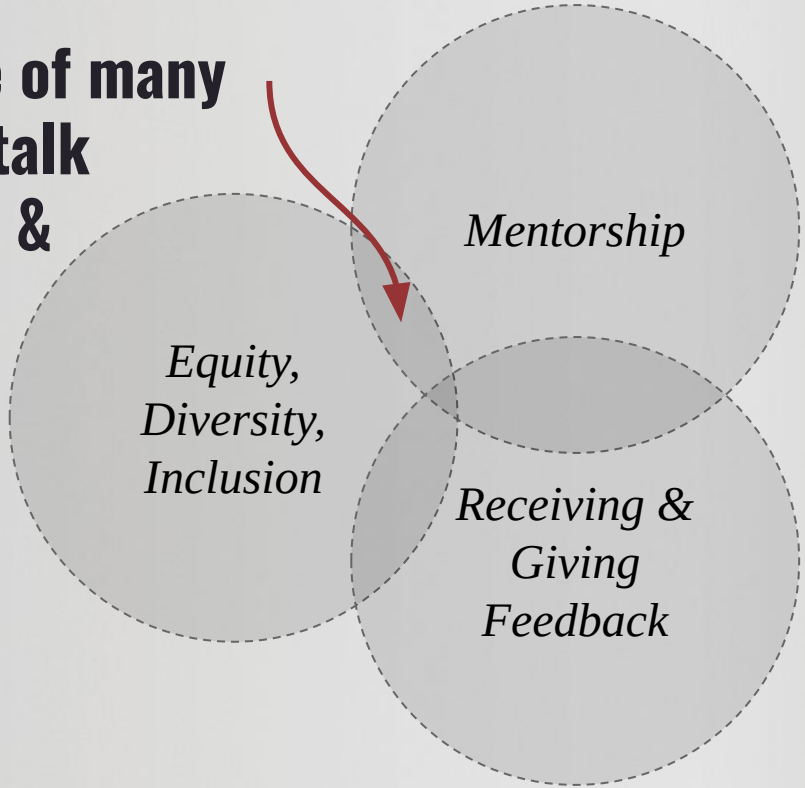
STARTneuro

The scientific enterprise is built on a foundation of **trust**. Society trusts that scientific research results are an honest and accurate reflection of a researcher's work. Researchers equally trust that their colleagues have *gathered data carefully, have used appropriate analytic and statistical techniques, have reported their results accurately, and have treated the work of other researchers with respect*. When this trust is misplaced and the professional standards of science are violated, researchers are not just personally affronted—they feel that the base of their profession has been undermined.

- National Academies, *On Being a Scientist*

Trust is at the core of many of the topics we'll talk about this summer & beyond

… Ethics is not a *separate issue!*



Science is fundamentally a human endeavor, led by human decision making

We make decisions about:

- What research is worth doing
- How we analyze our data
- Which data we report
- How we share the data

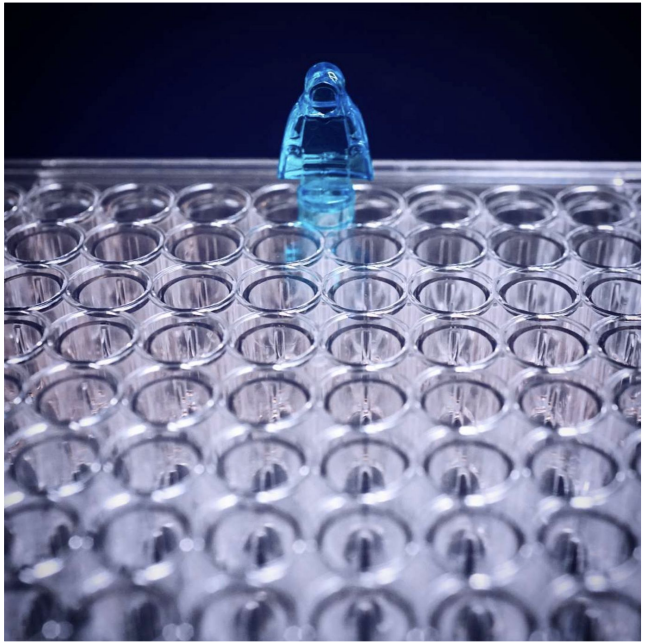
Core ethical questions

- How should research be conducted so as to meet our obligations to preserve and promote the integrity of research findings?
- How should researchers interact with one another to meet our obligations to other researchers?
- How should researchers interact with the larger communities, academic and public, to meet our obligations to the society in which we live and work?

(Unspoken) standards for scientific research

Researchers have an obligation to:

- honor the trust that their colleagues place in them
- maintain their own integrity
- act in ways that serve the public



@legobiologist

Goals for today

- Motivate the focus on research rigor & reproducibility
- Define research misconduct
- Discuss case studies relevant to doing biology research
- Provide resources for learning more, or inquiring about a possible issue

The reproducibility crisis

Ioannidis JPA (2005):
Why most published research findings are false.
PLoS Med 2(8): e124.

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. "Negative" is actually a misnomer, and 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 2×2 table, one gets $\text{PPV} = (1 - \beta)R/(R$

Bayer tried to replicate results of 67 studies in academic journals

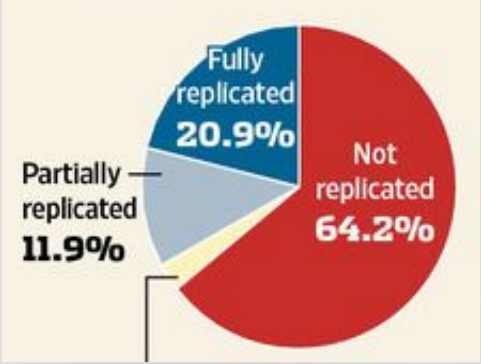


Figure from: https://www.drugabuse.gov/about-nida/noras-blog/2013/09/improving-reproducibility-transparency-in-biomedical-research

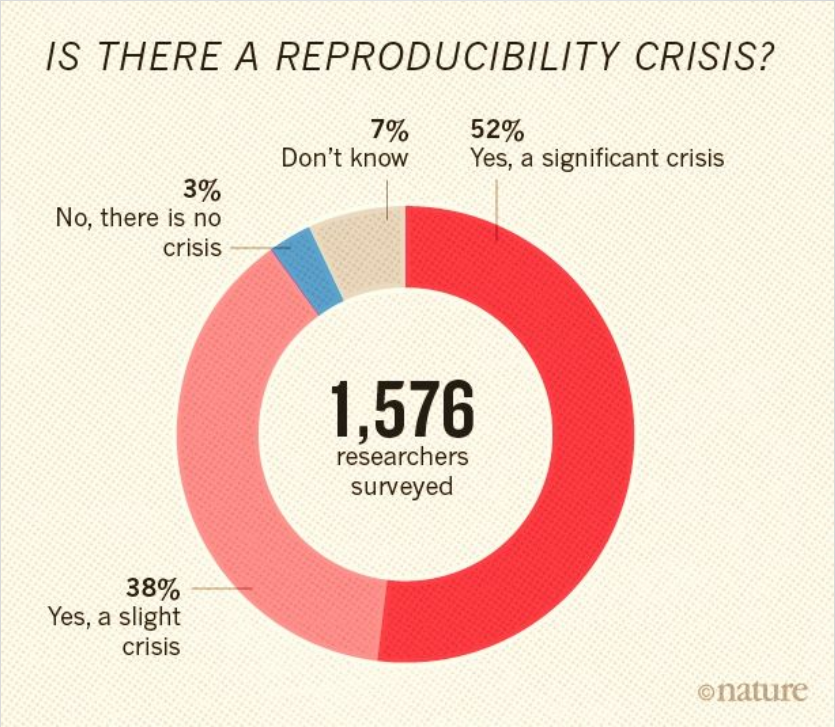
Amgen undertook a project to reproduce the results of more 53 "landmark" published studies

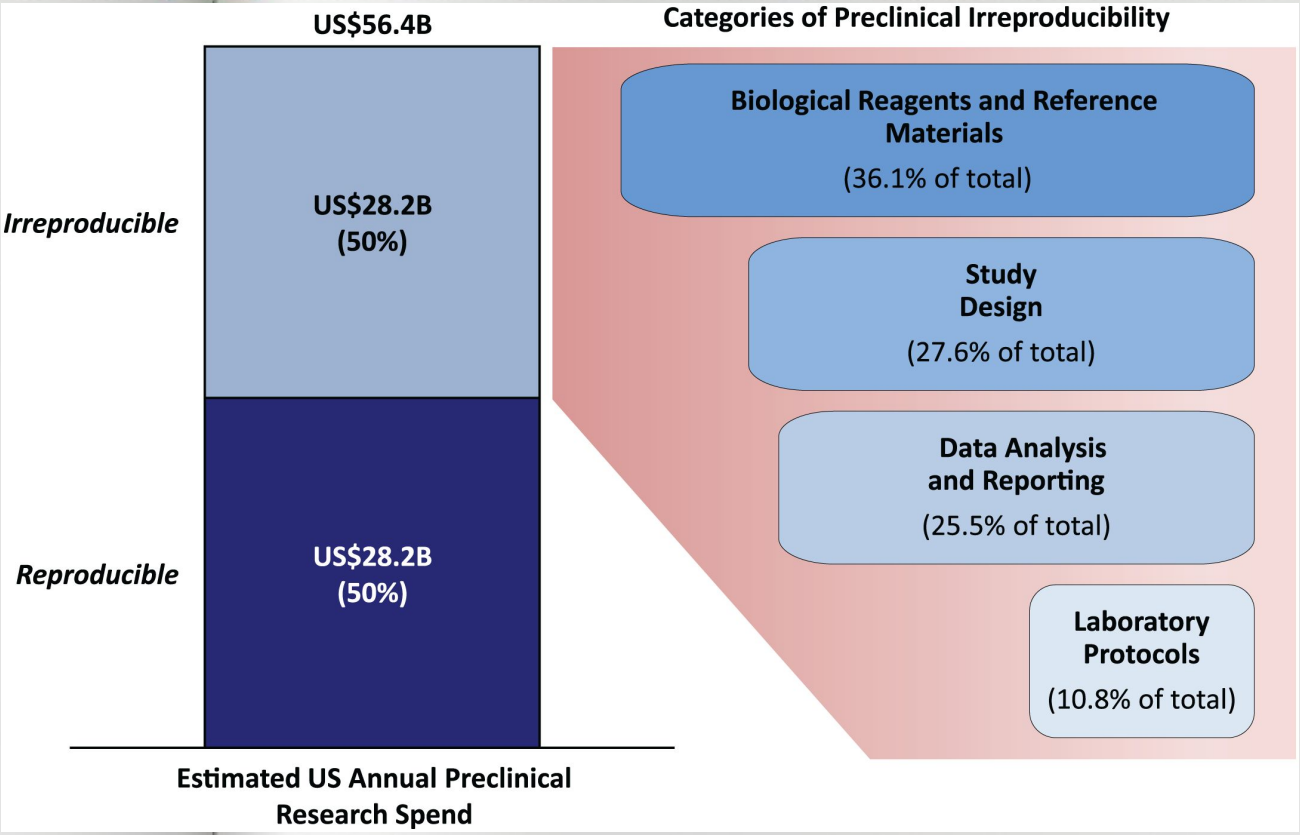
Only 11% were reproducible - even by the original researchers who had done the work

Begley CG and Ellis LM (2012): Drug development: Raise standards for preclinical cancer research. Nature 483:531–533

Is there a reproducibility crisis?

Baker M (2016):
Is there a reproducibility crisis?
Nature 533:452-454.





Many factors contribute to this crisis, but namely Reagents and Materials, ***Design, Data analysis and Reporting, and Protocols.***

Freedman et al. (2015): The Economics of Reproducibility in Preclinical Research. PLOS Biology

Scientific misconduct

Fabrication, **falsification**, or **plagiarism** in proposing, performing, or reviewing research, or in reporting research results.

All research institutions that receive federal funds must have policies and procedures in place to investigate and report research misconduct.

Research Integrity @ UCSD

Fabrication

making up data or results

Falsification

manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record

Plagiarism

the appropriation of another person’s ideas, processes, results, or words without giving appropriate credit

(As defined by the U.S. Office of Science and Technology Policy)

Authorship is also an issue of ethics

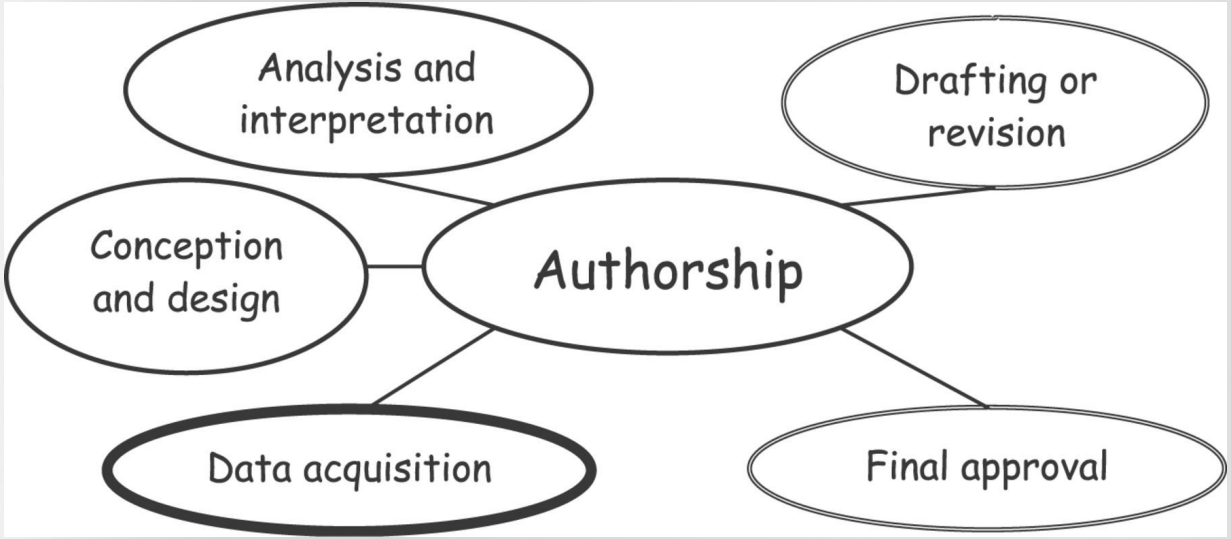
1. What are the criteria for authorship?
2. In what order should authors be listed?
3. How can credit be assigned if not by authorship?
4. Who decides?
5. What are the options for resolving a dispute about authorship?

UCSD Research Ethics Topics

ICMJE | Recommendations | Defining the Role of Authors and Contributors

No one wants to talk about authorship | by Ashley Juavinett | Medium

Authorship is also an issue of ethics



From [Ethics of Data Sharing and Reuse in Biology | BioScience | Oxford Academic]

Why scientists have an ethical obligation to share data

Obligation	Rationale
Replication	The ability to replicate results of analyses is a fundamental element of the scientific process, but for many types of time-sensitive environmental data, replication is possible only if the original data are available for reanalysis.
Human rights	Article 15 of the International Covenant on Economic, Social and Cultural Rights dictates that everyone has the right to “enjoy the benefits of scientific progress and its applications,” but failure to share data restricts that right.
Data preservation	Data that are not systematically archived are frequently lost as a result of computer failures, software obsolescence, or simple neglect.
Scientific progress	The scientific community, as a whole, benefits from the ability to discover, access, and analyze diverse data sets.
Data integrity	Multiple users make it more likely that deficiencies in data will come to light.
Public trust	In the face of controversy, the willingness to share data can be a key factor in increasing public trust in the results of scientific research.

From Ethics of Data Sharing and Reuse in Biology | BioScience | Oxford Academic

See also https://www.nature.com/articles/s41467-018-05227-z

Case study time

Is it plagiarism?

Professor Lee is writing a proposal for a research grant, and the deadline for the proposal submission is two days from now. To complete the background section of the proposal, Lee copies a few isolated sentences of a journal paper written by another author. The copied sentences consist of brief, factual, one-sentence summaries of earlier articles closely related to the proposal, descriptions of basic concepts from textbooks, and definitions of standard mathematical notations. Lee adds a one-sentence summary of the journal paper and cites it.

Questions for discussion

1. Does the copying of a few isolated sentences in this case constitute plagiarism?

2. By citing the journal paper, has Lee given proper credit to the other author?

We can also consider the following:

WHO: Who (individuals, institutions, a field of research, society) is affected?

CONFLICTS: What interest(s) (material, financial, ethical, other) does each party have in the situation? Which interests are in conflict?

ACTIONS TAKEN: Were the actions taken by each of the affected parties acceptable (ethical, legal, moral, or common sense)? If not, are there circumstances under which those actions would have been acceptable? Who should impose what sanction(s)?

OPTIONS: What other courses of action are open to each of the affected parties? What is the likely outcome of each course of action?

YOUR CHOICE: What course of action would you take, and why?

PREVENTION: What actions could have been taken to avoid the conflict?

Case study time!

In your group:

- Read the case study
- Respond to the discussion questions
- Be prepared to summarize your case & your discussion

Case studies found here:
Ethics Case Studies

Goals for today

- During class:
  - Motivate the focus on research rigor & reproducibility
  - Define research misconduct
  - Discuss case studies to doing biology research
  - Provide resources for learning more, or inquiring about a possible issue
- After class
  - Develop a prevention strategy

Additional resources

On Being a Scientist: A Guide to Responsible Conduct in Research: Third Edition | The National Academies Press

https://ethics.ucsd.edu/resources/instructor-resources/index.html#Course-Resources

Follow @UCSD_EthicsProg on Twitter!