UNIVERSITY OF GOTHENBURG
KREFTING RESEARCH CENTRE

Thinking REPRODUCIBILITY in Your Research Work

13th August 2020

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University of Gothenburg, Sweden

Aims of talk

- Motivate you into field of reproducible research
- Emphasize importance of thinking reproducibility throughout research
- Highlight consequences of irreproducibility
- Point to tools and platforms to enhance reproducibility in your research

First things First: What is science/research?

- **SCIENCE:** “Any system of knowledge that is concerned with the physical world and its phenomena and that entails unbiased observations and systematic experimentation. In general, a science involves a pursuit of knowledge covering general truths or the operations of fundamental laws” (Encyclopedia Britannica: https://www.britannica.com/)

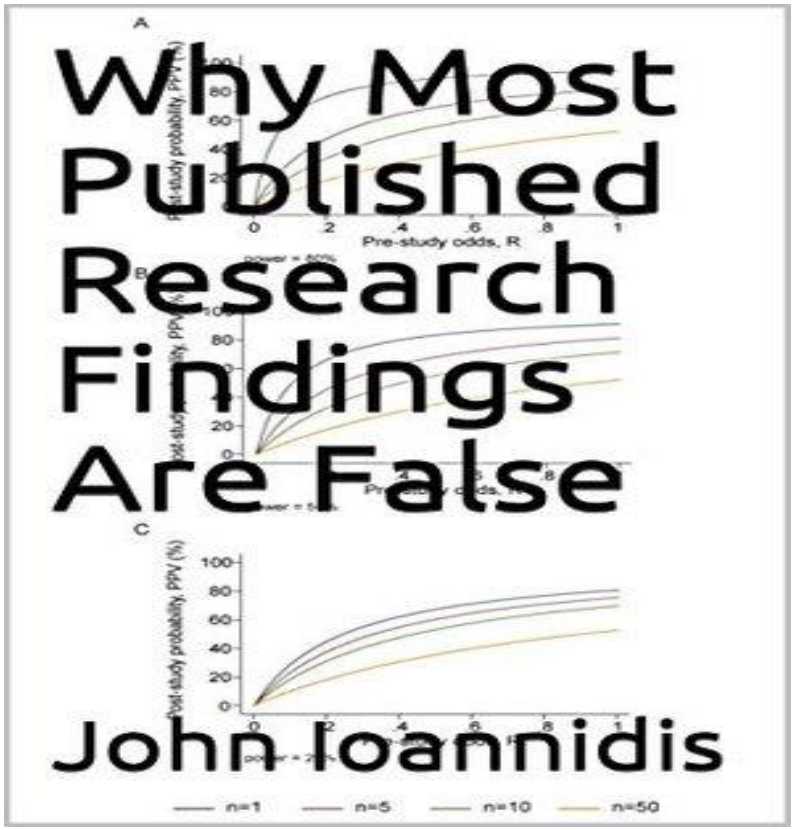
- **RESEARCH:** “A process of systematic inquiry that entails collection of data; documentation of critical information; and analysis and interpretation of that data/information, in accordance with suitable methodologies set by specific professional fields and academic disciplines” (Hampshire College: https://www.hampshire.edu/dof/what-is-research)

Why do scientists do research?
What is the end goal of my research?
These are fundamental questions
Often not considered by many scientists

Science's greatest motivation: a safer society (UNESCO)

- Science: greatest collective endeavor. Contributes to:
  - Longer and healthier life: monitors our health, provides medicine to cure our diseases, alleviates aches and pains
  - Provision of our basic needs: water, food, energy, clean air
  - Making our lives more fun: sports, music, entertainment and communication technology
  - Creating new knowledge to improve education and quality of our lives
- Science generates solutions for everyday life
- Science must respond to societal needs and global challenges.

But does (all) science fulfil its mandate?



"Most research findings are false for most research designs and for most fields"

Ioannidis 2005; PLoS Med 2(8): e124.

Some case studies of bad science

Pressure:
publish or perish

Stem-Cell Scandal

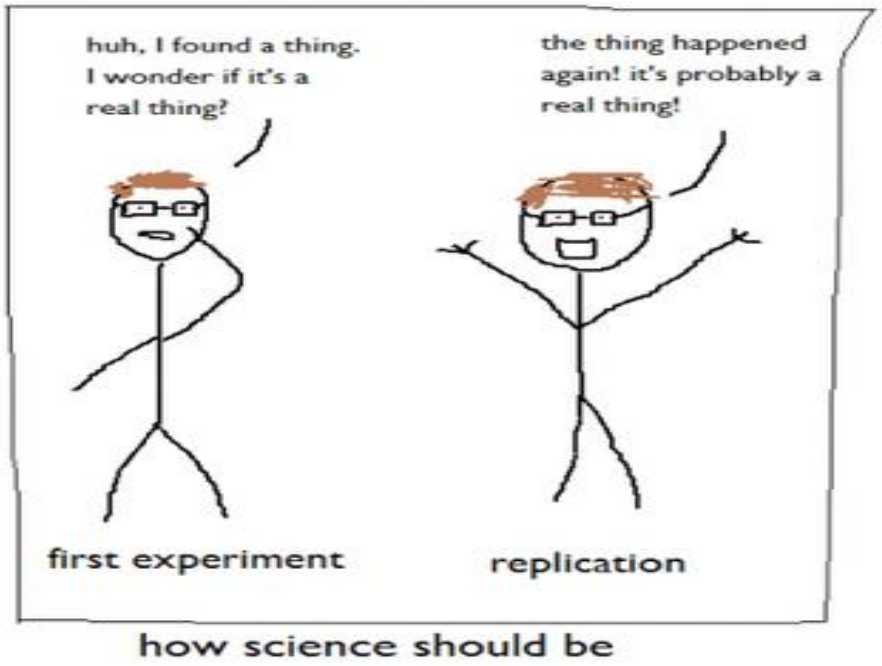
Diederik Stapel

Child Co-Authors in Korea

https://retractionwatch.com/

Replication

- Duplicating results of prior study using independent investigators, methods, data, equipment, and protocols
  (Peng et al. Am J Epidemiol 2006; 163: 783-789)
- Gold standard of scientific investigation
- Credibility of scientific claim depends on its replicability
  - Not on authority of investigators



- Replication often impossible
  - Differences between original and replicating study
    - Time
    - Setting
    - Investigators
    - Measurements
    - Protocol execution
    - Costs

Reproducibility

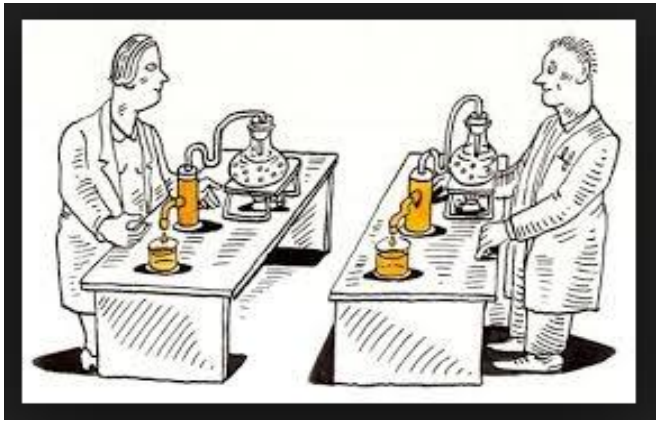
- The ability of an investigator to duplicate the results of a prior study using the same methods as were used by the original investigator

  Goodman et al. *Sci Transl Med* 2016; 8: 341ps12

- Minimum standard in place of replication

- Synonyms: Transparency, validation Verification. Processing trail, Open science, Corroboration

IF A JOB IS WORTH DOING, IT IS WORTH DOING TWICE



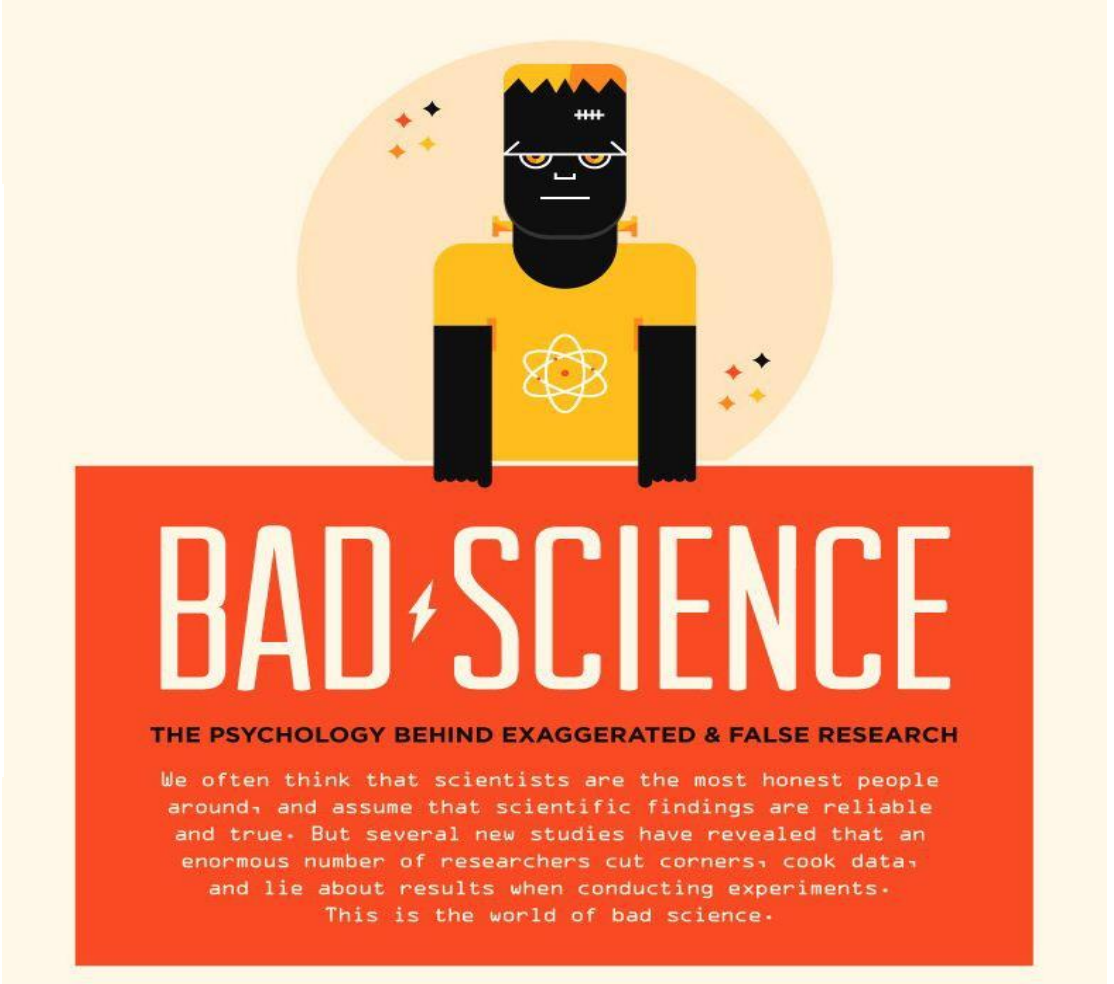
Russell. Nature 2013; 496:7

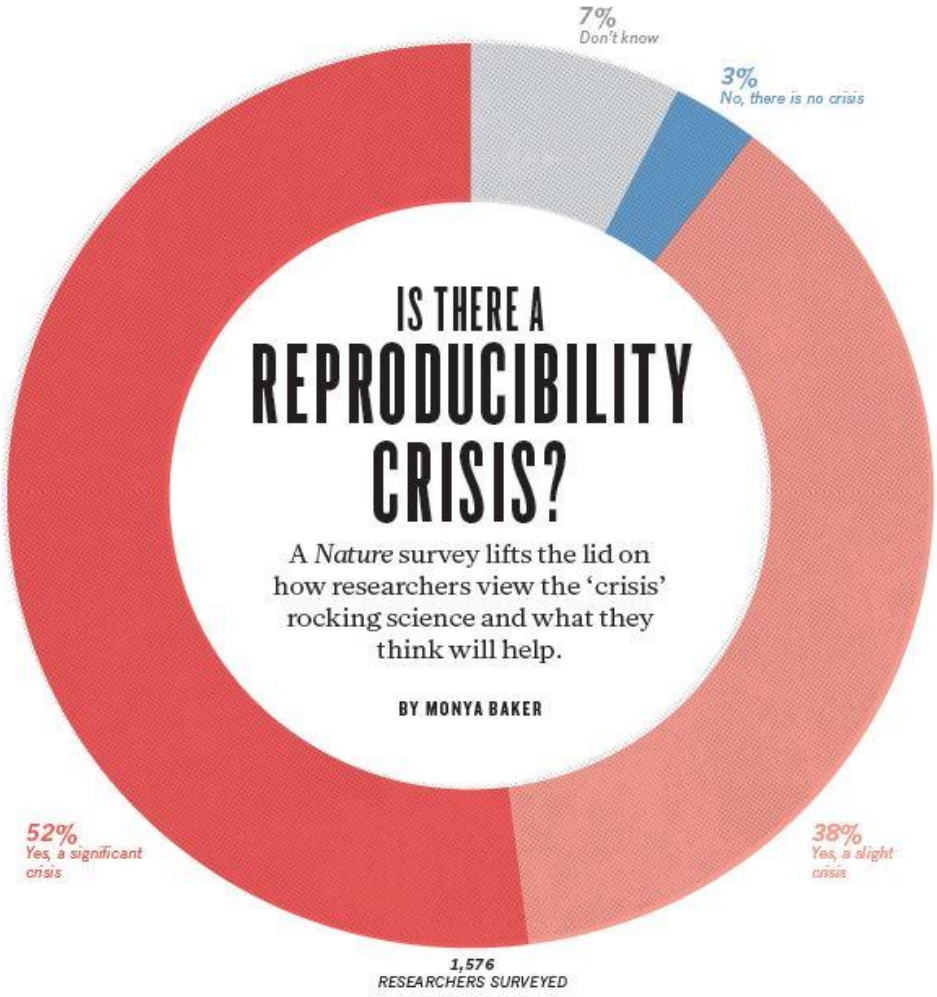
Reproducibility crisis?

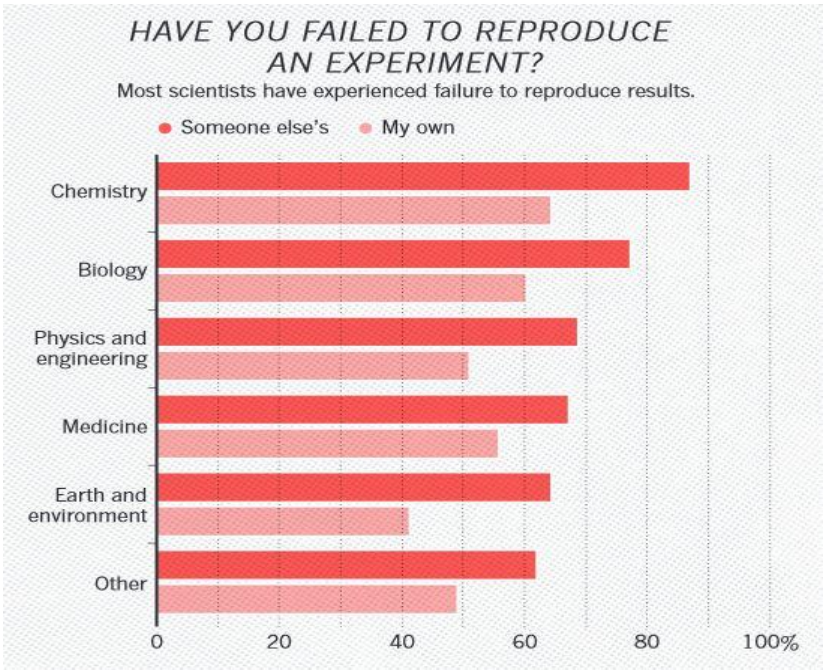
Why Most Published Research Findings Are False

John P. A. Ioannidis

Ioannidis 2005; PLoS Med 2(8): e124.







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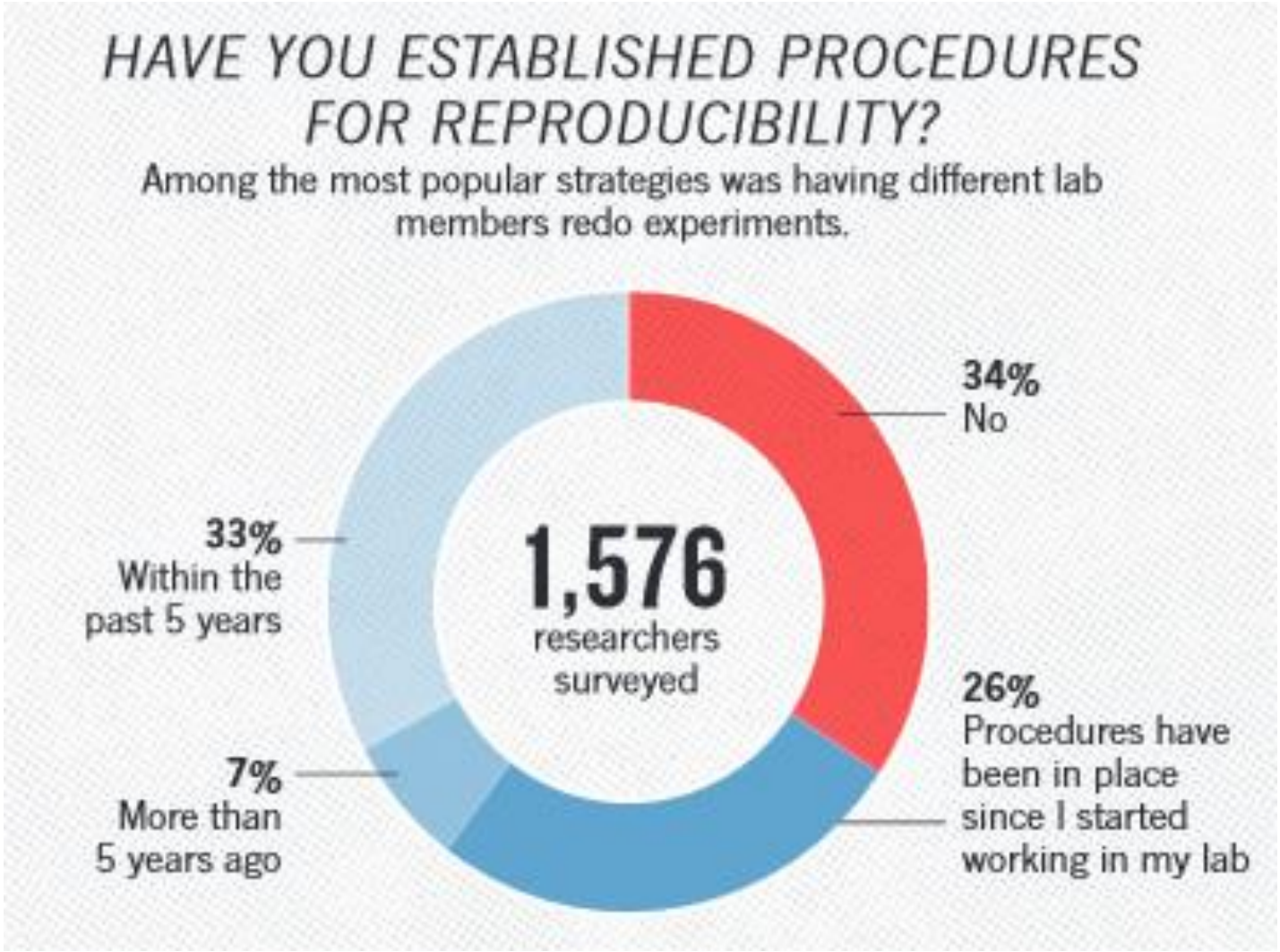

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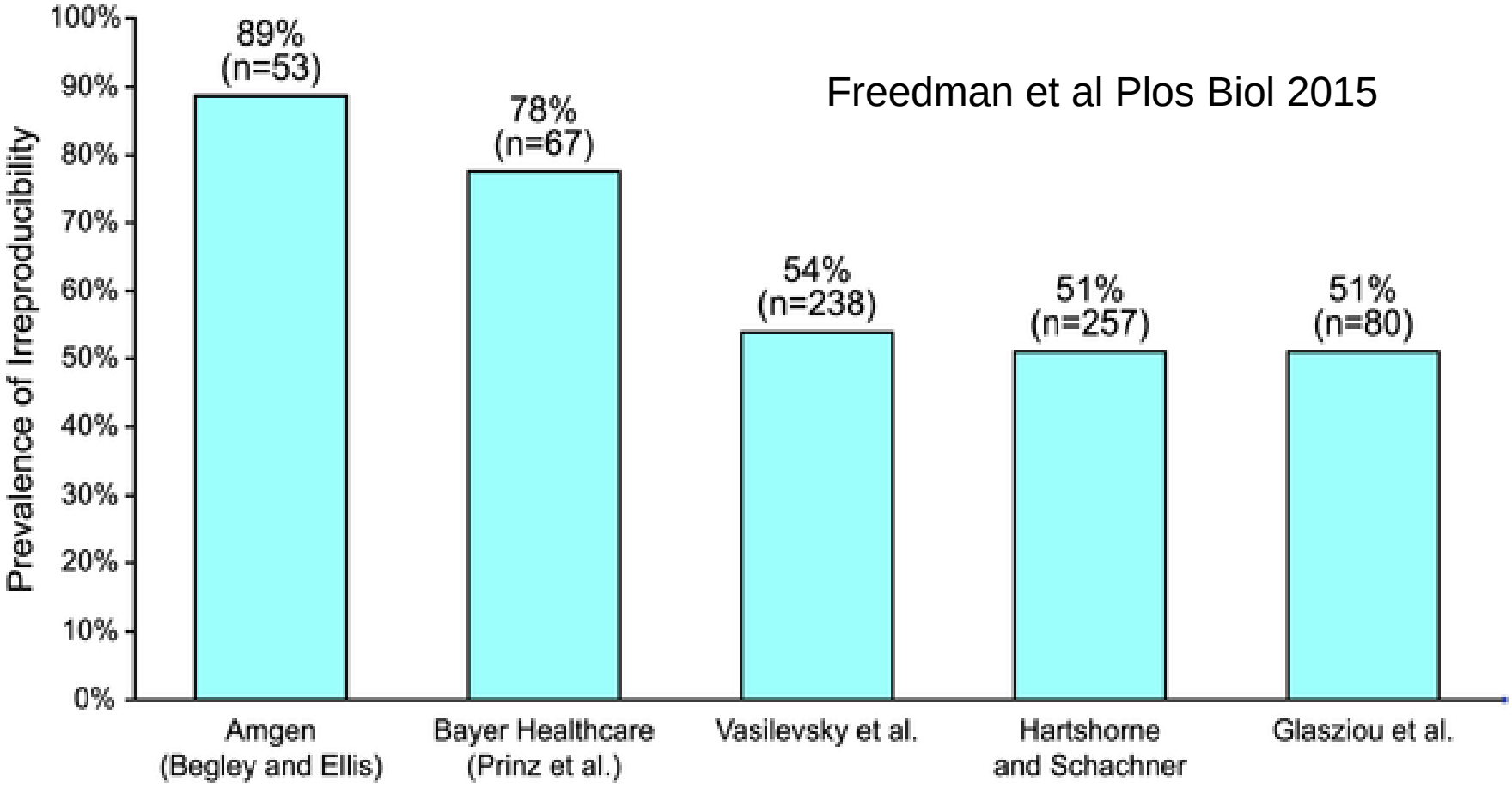
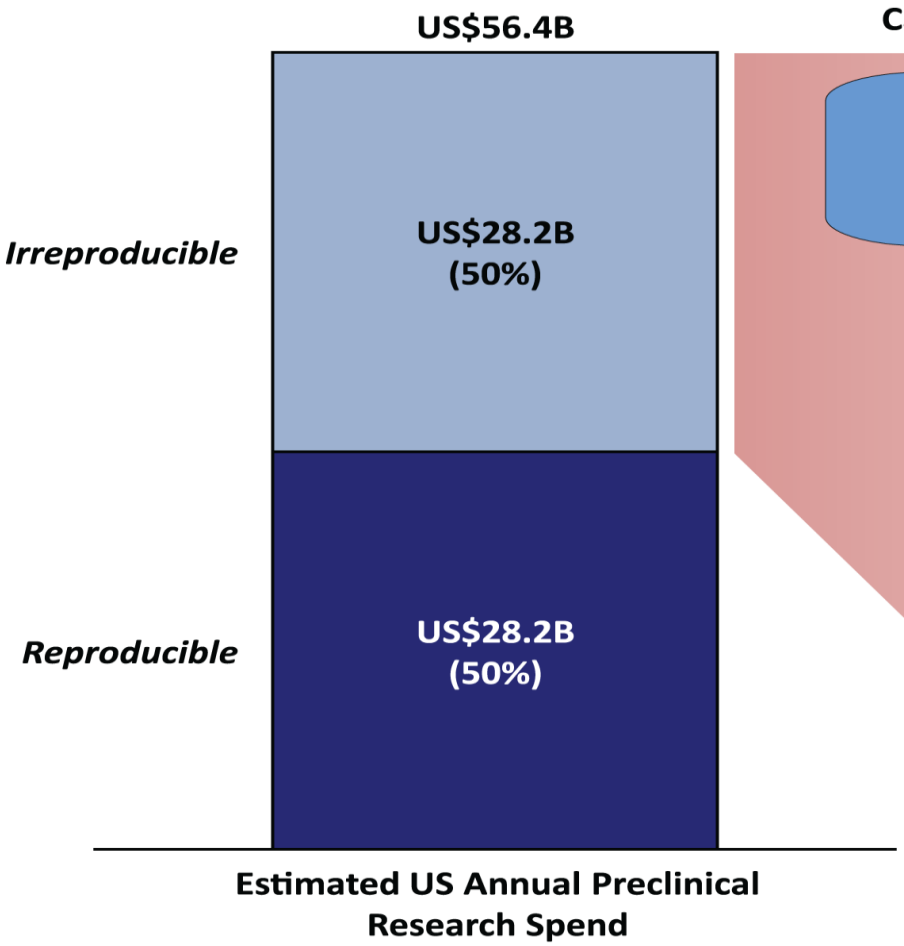
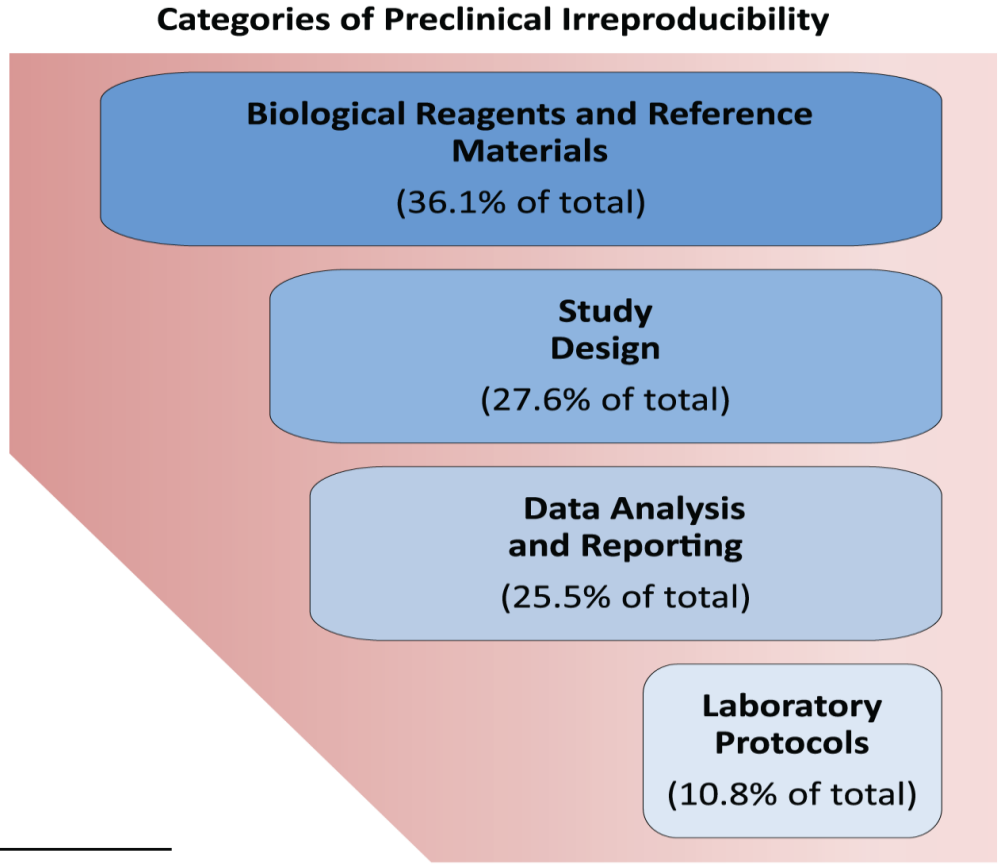
Prevalence of irreproducibility



Freedman et al Plos Biol 2015

Economics of irreproducibility





Freedman et al Plos Biol 2015

Impacts of irreproducibility

- Undermines cumulative knowledge production
- False alarm – false positive findings
- Contributes to delay in development of therapy
- Increases costs of therapeutic development
- Meta-analyses of studies may lead to wrong conclusion;
- Negative effects on medical guidelines
- Clinical trials based on faked data can lead to:
  - Harm
  - Wastage of resources and time
- Integrity of science
- Undermines public trust of science
- Career of perpetrators and co-authors

What can be done?

"NOT EVERY PAPER NEEDS TO BE MEDICALLY RELEVANT BUT THEY SHOULD ALL BE REPRODUCIBLE.

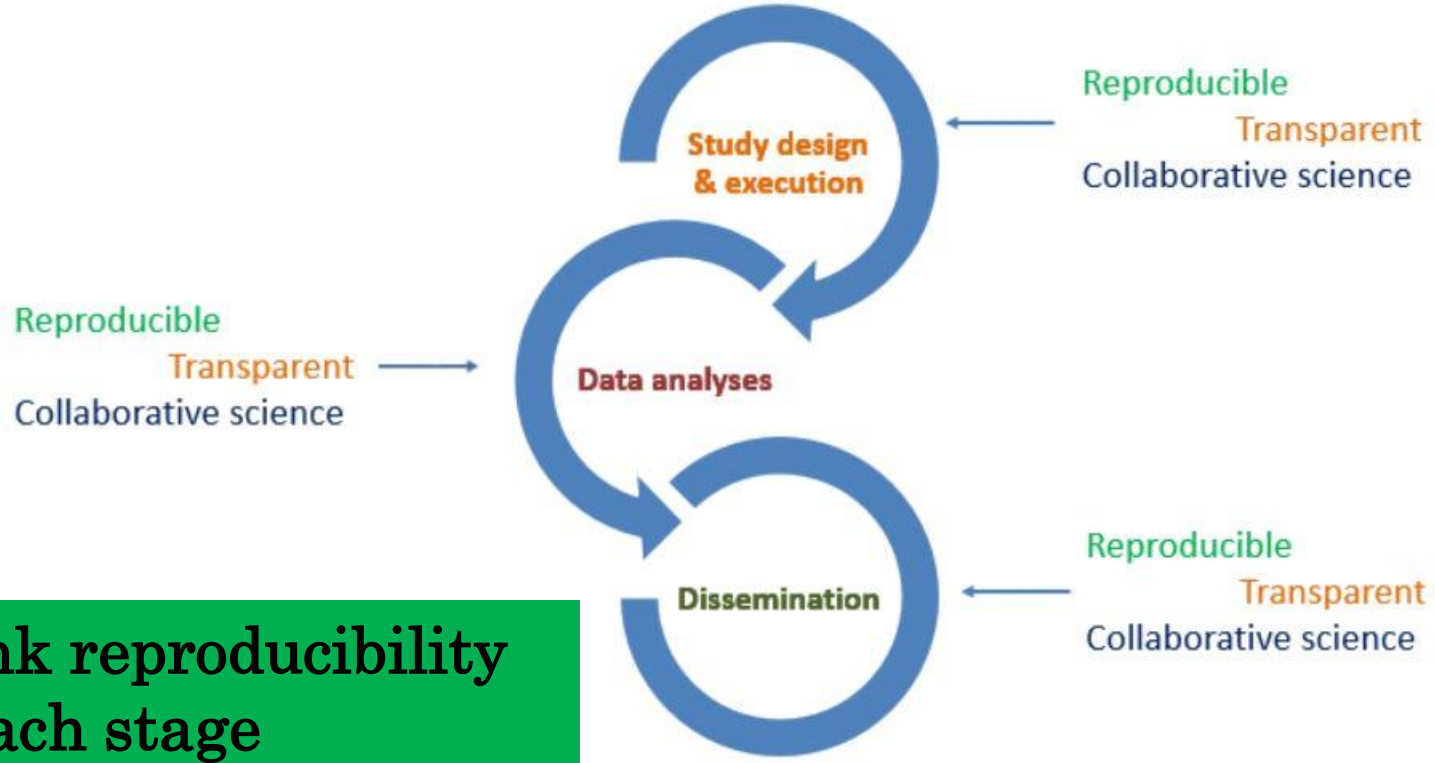
Russell. Nature 2013; 496:7

"REPRODUCIBILITY IS LIKE BRUSHING YOUR TEETH. ONCE YOU LEARN IT, IT BECOMES A HABIT."

Baker. Nature 2016; 533: 452-454

How to enhance reproducibility

- Reproducibility affects all research stages



Think reproducibility at each stage

How to Make More Published Research True

John P. A. Ioannidis[1,2,3,4]*

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PLoS Med 2014; 11(10): e1001747

Box 1. Some Research Practices that May Help Increase the Proportion of True Research Findings

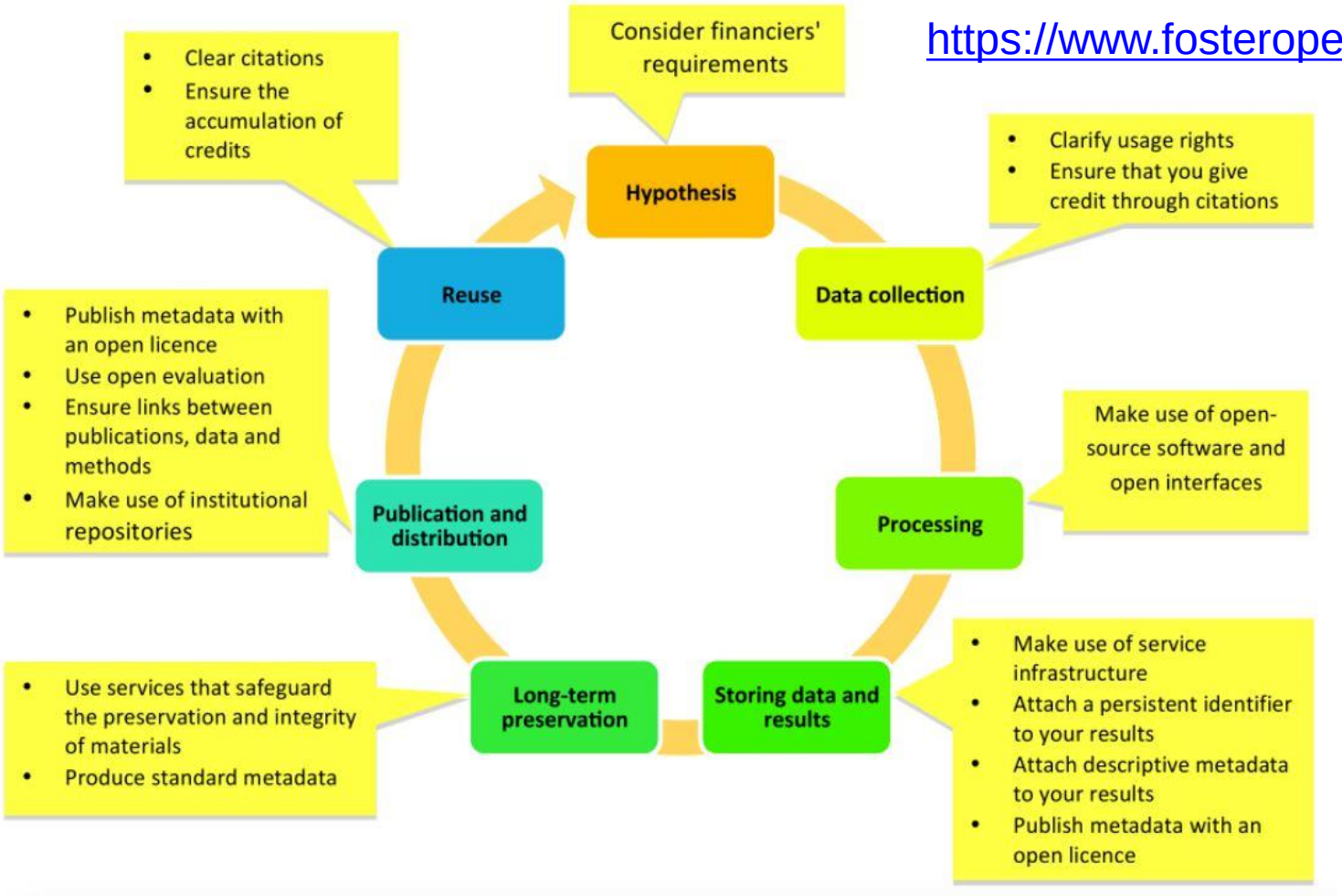
- Large-scale collaborative research
- Adoption of replication culture
- Registration (of studies, protocols, analysis codes, datasets, raw data, and results)
- Sharing (of data, protocols, materials, software, and other tools)
- Reproducibility practices
- Containment of conflicted sponsors and authors
- More appropriate statistical methods
- Standardization of definitions and analyses
- More stringent thresholds for claiming discoveries or "successes"
- Improvement of study design standards
- Improvements in peer review, reporting, and dissemination of research
- Better training of scientific workforce in methods and statistical literacy

Reproducibility and reliability of biomedical research: improving research practice

UK Academy of Medical Sciences Symposium report, October 2015

https://acmedsci.ac.uk/file-download/38189-56531416e2949.pdf

Open science initiatives



https://www.fosteropenscience.eu/

Study design: register protocol

https://cos.io/prereg/

Develop, register, publish protocol prior to study conduct

Preregistration makes your science better by increasing the credibility of your results

Helps prevents Publication bias

Study design: register protocol

ClinicalTrials.gov https://clinicaltrials.gov/

https://www.clinicaltrialsregister.eu/ EU Clinical Trials Register

ENEPP European Network of Centres for Pharmacoepidemiology and Pharmacovigilance http://www.encepp.eu/encepp/studiesDatabase.jsp

https://www.crd.york.ac.uk/prospero/ PROSPERO International prospective register of systematic reviews

Why register study protocol?

- Open science practice
- Promotes transparency and reliability of results
- Helps prevent certain research practices:
  - Flexible analyses
  - Post-hoc analyses
  - Selective outcome reporting, p-hacking, cherry picking
  - HARKing - hypothesizing after the results are known
- Informs peers of ongoing research and enhances collaboration
- Increased likelihood of publication

Reproducibility in data analysis

"A study is reproducible if all of the code and data used to generate the numbers and figures in the paper are available and exactly produce the published results"

Leek & Jager. Annu Rev Stat 2017; 4:109-22

Reproducibility in data analysis

BMJ

BMJ 2012;344:e4383 doi: 10.1136/bmj.e4383 (Published 26 June 2012)

EDITORIALS

Open science and reproducible research

New reports call for scientists to share data and publishers to embrace open access

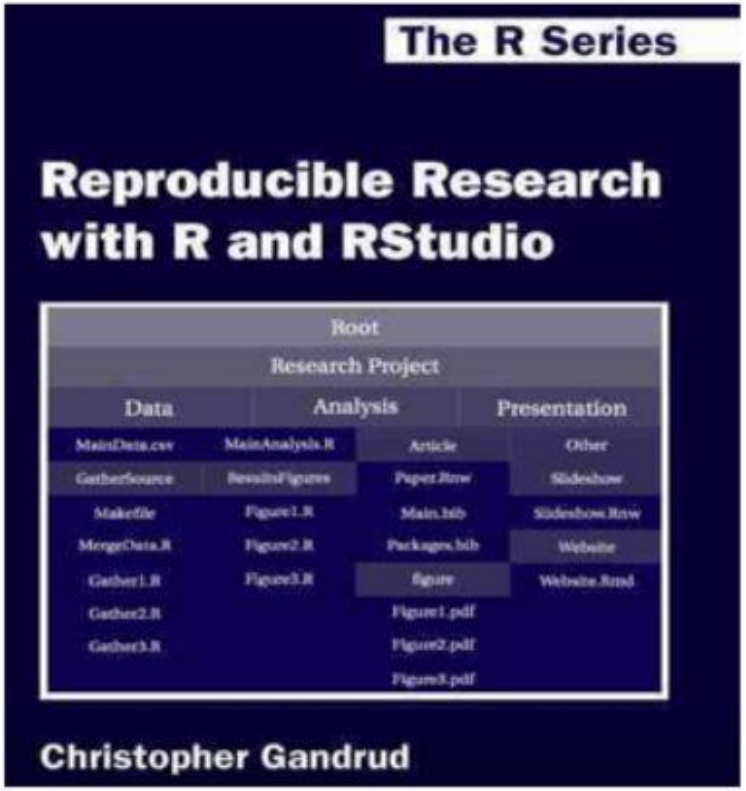
"Scientists should communicate the data they collect and the models they create, to allow free and open access, and in ways that are intelligible, assessable and usable for other specialists.. . . Where data justify it, scientists should make them available in an appropriate data repository."

Reproducibility in data analysis

Item	Requirement
Data	Study data set made available, if possible
Code	Code used for results, tables, figures made available in human readable form. Software used also available
Documentation	Sufficient details of the analyses steps and code to help others repeat them
Distribution	Above made available through a platform others can have access to them

Reproducibility across statistical software

- Good developments in R, Stata, SAS
  - Goal: bringing statistical code, data, and presentation together in a way for others to easily follow
    - Automate the process
    - Reduce human errors
  - Computationally advanced
  - Currently used primarily by those in statistics, engineering, computer sciences



Develop an analysis plan

- Detailed outline of your analyses
- A recipe: step-by-step analysis decisions
- If possible, publish a protocol
- If possible, register your protocol
- Consult with investigators / collaborators

Data editing

- Clean and code your data before analyses
- Data editing: careful scrutiny of raw data for errors
- Code variables sensibly
- Code variables in a reproducible way
  - Data coding syntaxes
  - If possible, publish syntaxes alongside paper
- Sensible management of data files crucial
- Sensible choice of categorization and variable transformation

Reporting (dissemination) and reproducibility

THE EQUATOR NETWORK:

https://www.equator-network.org/

Diversifying peer review

- Preprint platforms – facilitating easy sharing and discovery of research before publication
  - arXiv - physical sciences
  - bioRxiv and PeerJ - life sciences
  - engrXiv – engineering
  - PsyArXiv – psychology
  - SocArXiv - social sciences)
- Post-publication peer review platforms
  - PubMed Commons
  - PubPeer

Ethos of scientific research

- Robert K. Merton, 1942
- Most influential discourse of values of modern scientific research
- Articulated four core ethos (values)
  - Universalism
  - Communality
  - Disinterestedness
  - Organized skepticism

Universalism

- Scientific findings are not personal
  - “pre-established impersonal criteria.”
- To be valid, should not depend on investigator’s
  - Personal
  - Social
  - Political
  - National characteristics/affiliations
- Science is anti-authoritarian: idea acceptance not because of the qualities of its protagonist
  - With right training, anyone can contribute to science

Communality

- Evidence generation should be through:
  - Active collaboration within the scientific community
  - Open exchange of ideas
  - Discussion and consensus
  - Sharing of evidence
- Secrecy is antithesis of scientific research
- Scientific research is not motivated by commercialization

Disinterestedness

- Scientific research should be devoid of personal interest
  - Monetary motivations
  - Other interests
- Overarching motivation should be to uncover the truth

Organized skepticism

- Scientists should not take findings at face value
- Scrutiny should be strictly part of the process
- Active peer review process indispensable
- Replication/reproducibility indispensable