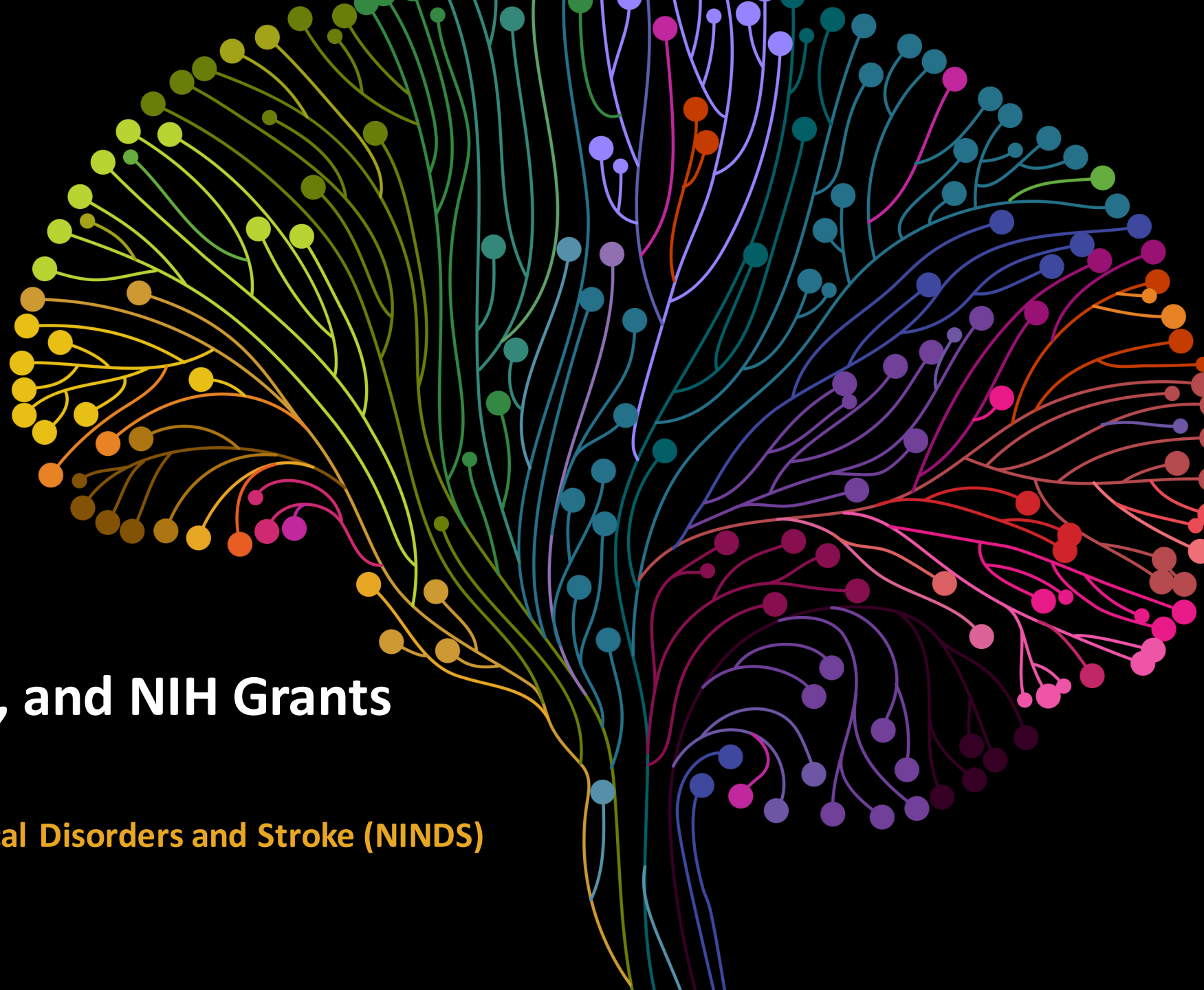


Rigor, Transparency, and NIH Grants

Devon Crawford, Ph.D.

Office of Research Quality

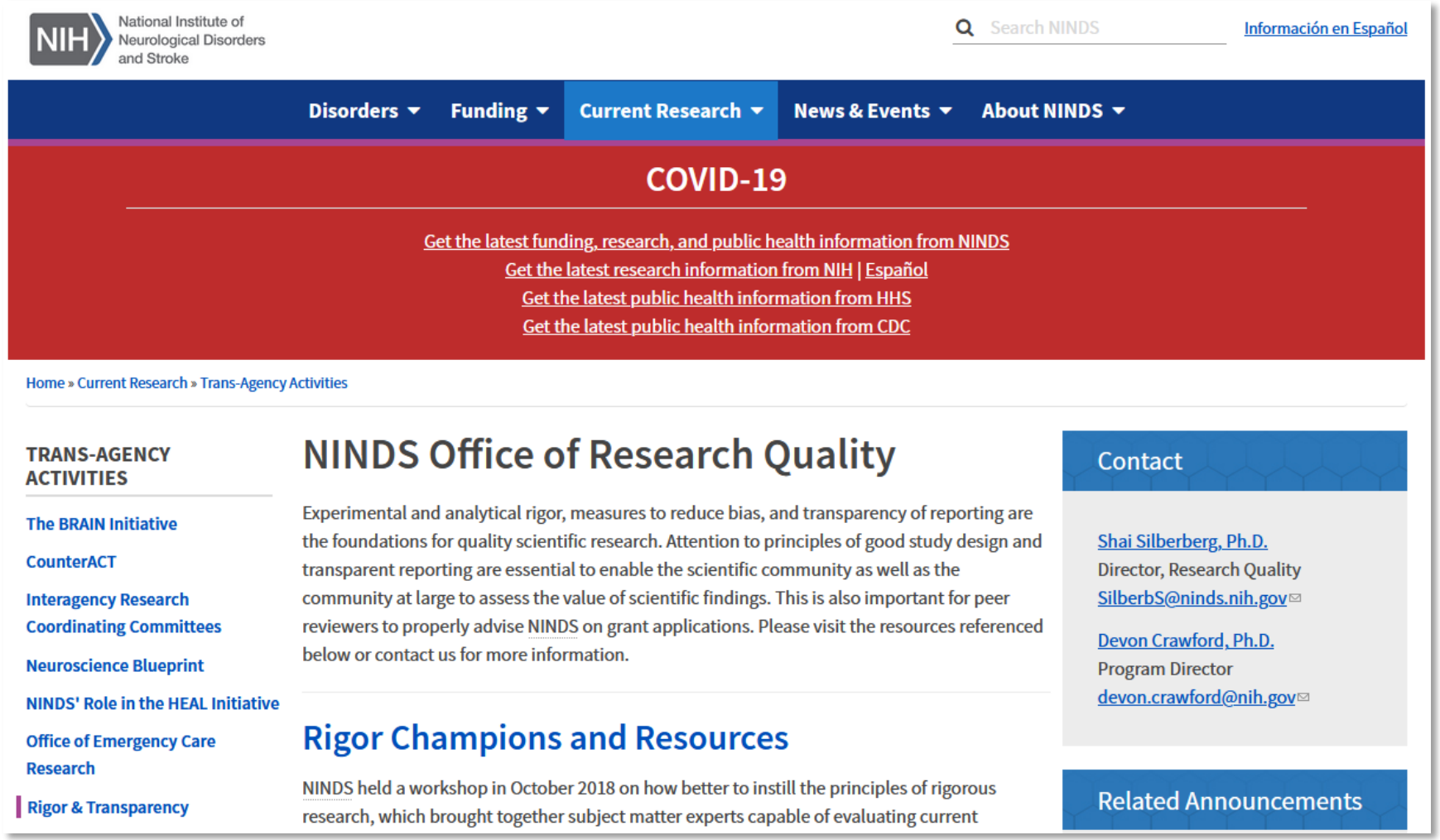
National Institute of Neurological Disorders and Stroke (NINDS)

National Institute of
Neurological Disorders
and Stroke

Disclaimer

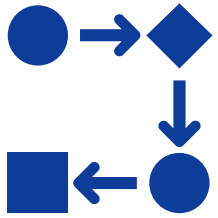
- Any opinions expressed in this presentation are my own and do not reflect the views of the National Institutes of Health, the Department of Health and Human Services, or the United States government.

NINDS Office of Research Quality

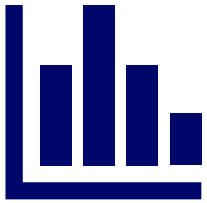


https://www.ninds.nih.gov/Current-Research/Trans-Agency-Activities/RigorAndReproducibility

Reproducibility and Replicability



- **Reproducibility**: obtaining consistent results using the same input data, computational steps, methods and code, and conditions of analysis. This definition is synonymous with computational reproducibility [NASEM]



- **Replicability**: obtaining consistent results across studies aimed at answering the same scientific question, each of which has obtained its own data [NASEM]

National Academies of Sciences, Engineering, and Medicine, *Reproducibility and Replicability in Science* 2019

Rigor and Transparency

- **Scientific Rigor**: strict application of the scientific method to ensure unbiased and well-controlled experimental design, methodology, analysis, interpretation and reporting of results [NIH definition]

- **Transparency**: reporting all relevant details about how an experiment was planned, executed, analyzed, and interpreted (including unexpected and inconvenient outcomes!)

We All Have Unconscious Bias

Francis Bacon

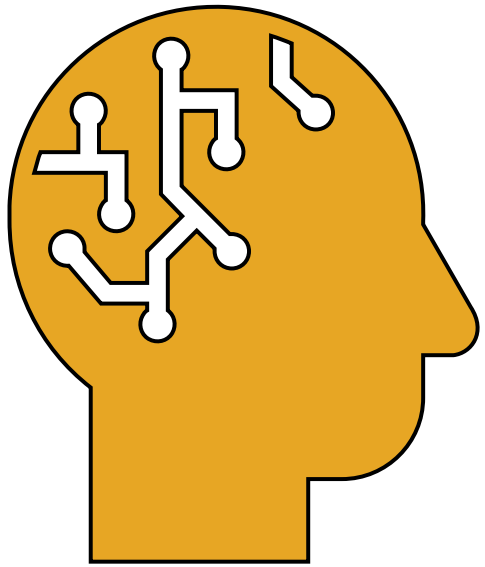
"[T]he human *understanding* when it has once adopted an opinion … draws all things else to *support and agree with it*. And though there be a greater number and weight of instances to be found on the other side, yet these it either neglects and despises, or else by some distinction sets aside and rejects; in order that by this great and pernicious predetermination the authority of its *former conclusions may remain inviolate*."

Novum Organum, 1620
Spedding, Ellis, and Heath Edition

Definition of Experimental Bias

"Bias is *unintentional* and *unconscious*. It is defined broadly as the *systematic erroneous association* of some characteristic with a group in a way that distorts a comparison with another group."

"The potential for bias to affect results and interpretation cannot be addressed by a simple process. … The process is more complicated and involves *making everything equal during the design, conduct and interpretation of a study, and reporting those steps in an explicit and transparent way*."

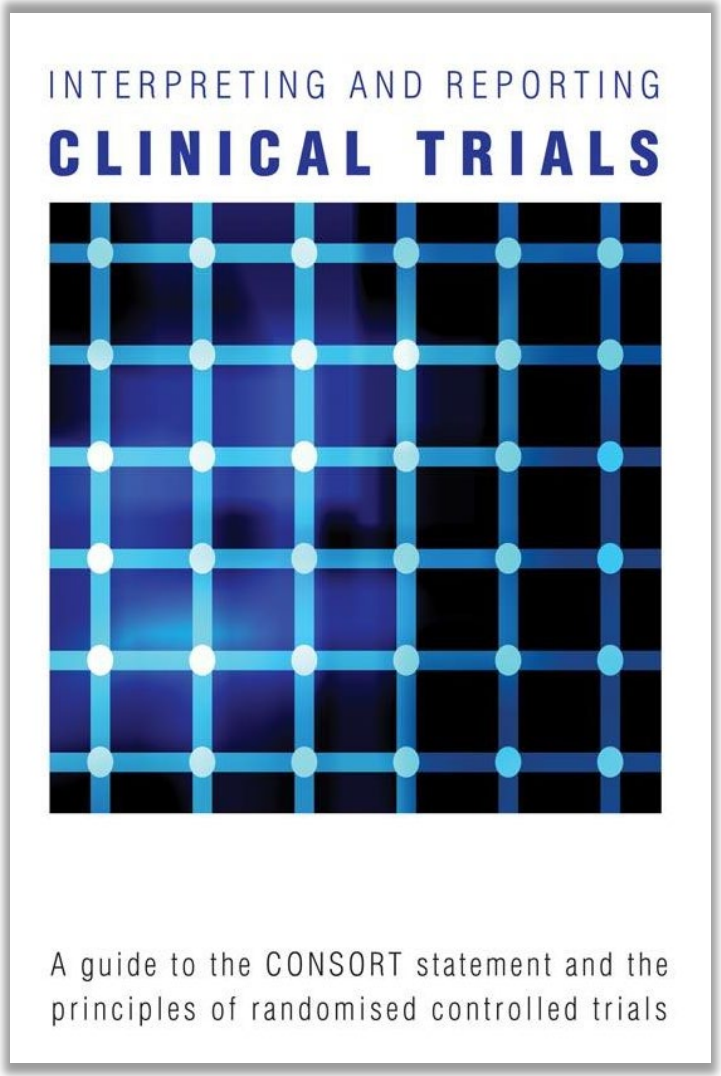


Ransohoff, *Nat Rev Cancer* 2005; 5: 142

CONSORT Statement: Guidelines for Reporting Clinical Trials

"*[R]andomised trials can yield biased results if they lack methodological rigour.*

To assess a trial accurately, readers of a published report need complete, clear, and *transparent* information on its *methodology and findings*."

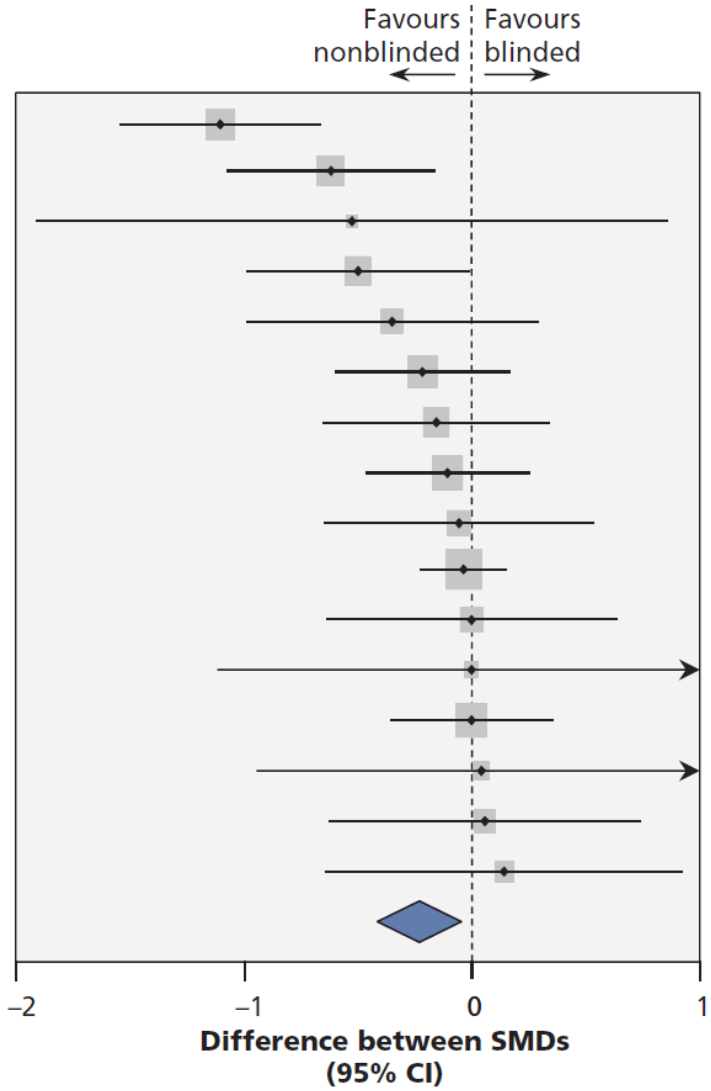


Schulz *et al.*, *PLOS Medicine* 2010; 7: 1

Unblinded Clinical Trial Outcome Measures Inflate Outcomes

Blinded vs. unblinded assessors in the same study:

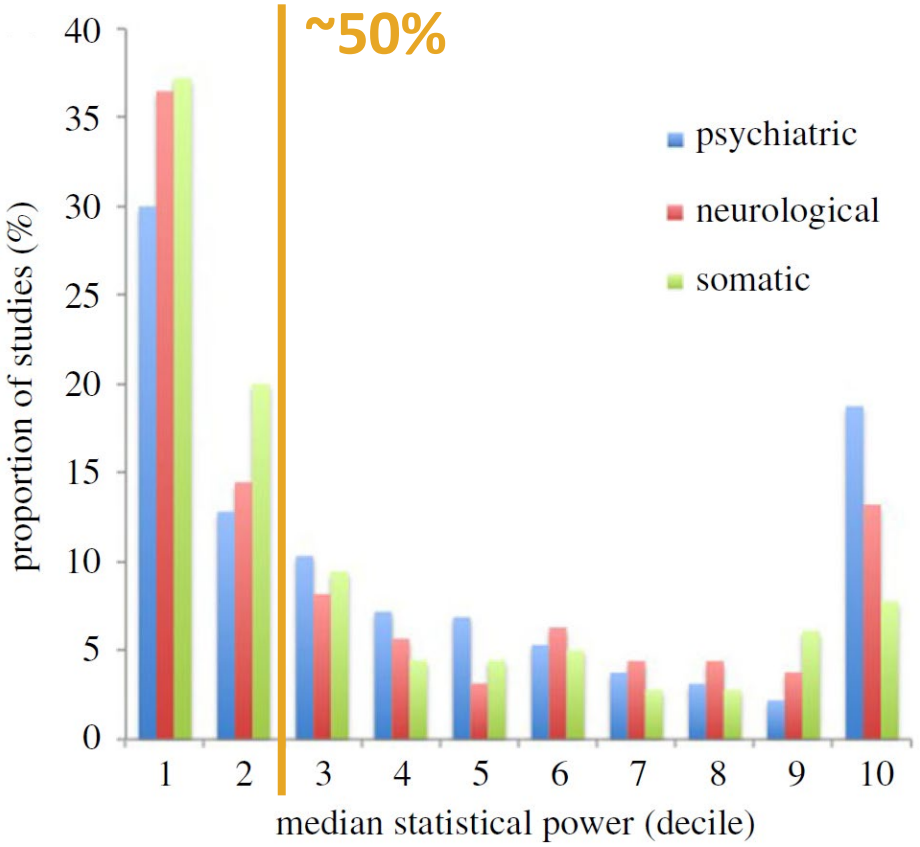
"In 10 trials (63%), the effect size point estimate was *more optimistic* as determined by the *nonblinded assessor*. … Standardized mean differences were exaggerated by a pooled standard deviation of 0.23."



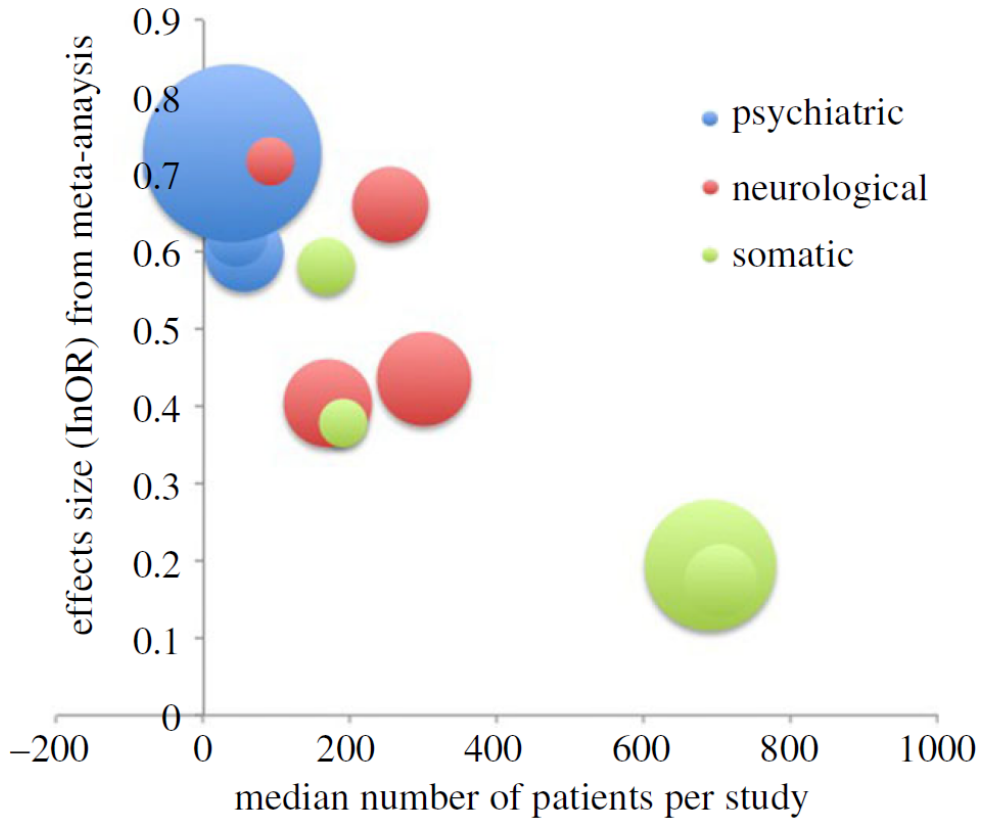
Hróbjartsson *et al.*, *CMAJ* 2013; 185: E201

Power & Sample Size in Mechanistic Human Studies

Power in 660 Meta-Analyses

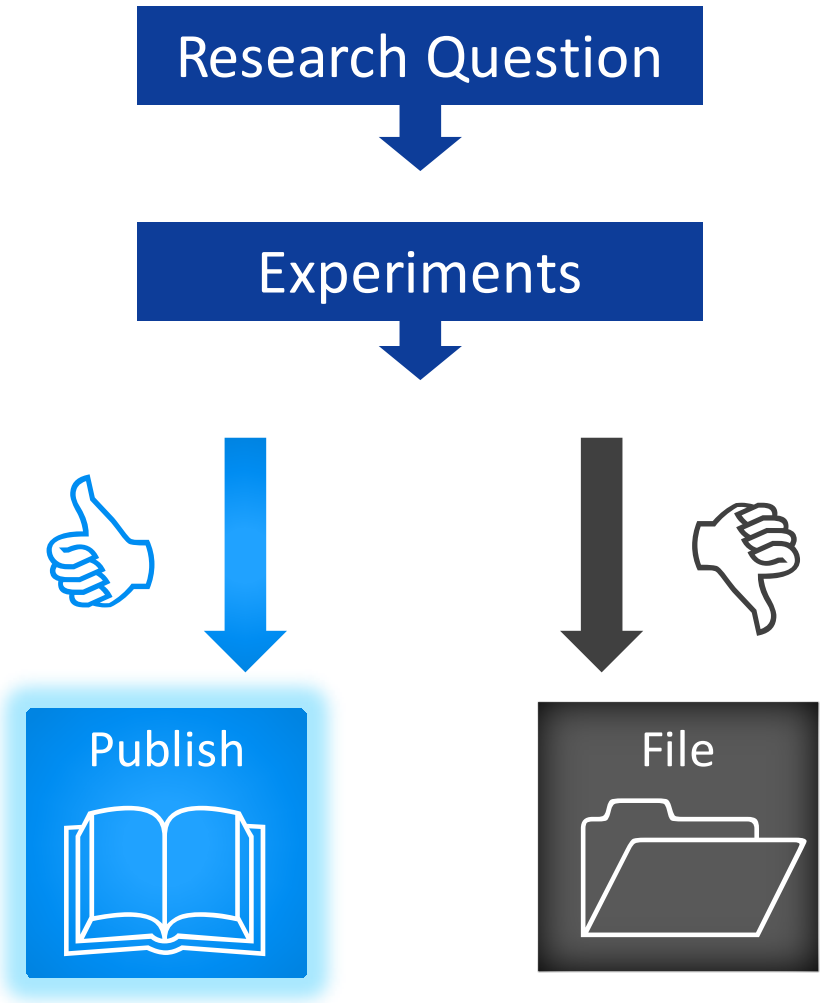


Effect Size vs. Sample Size

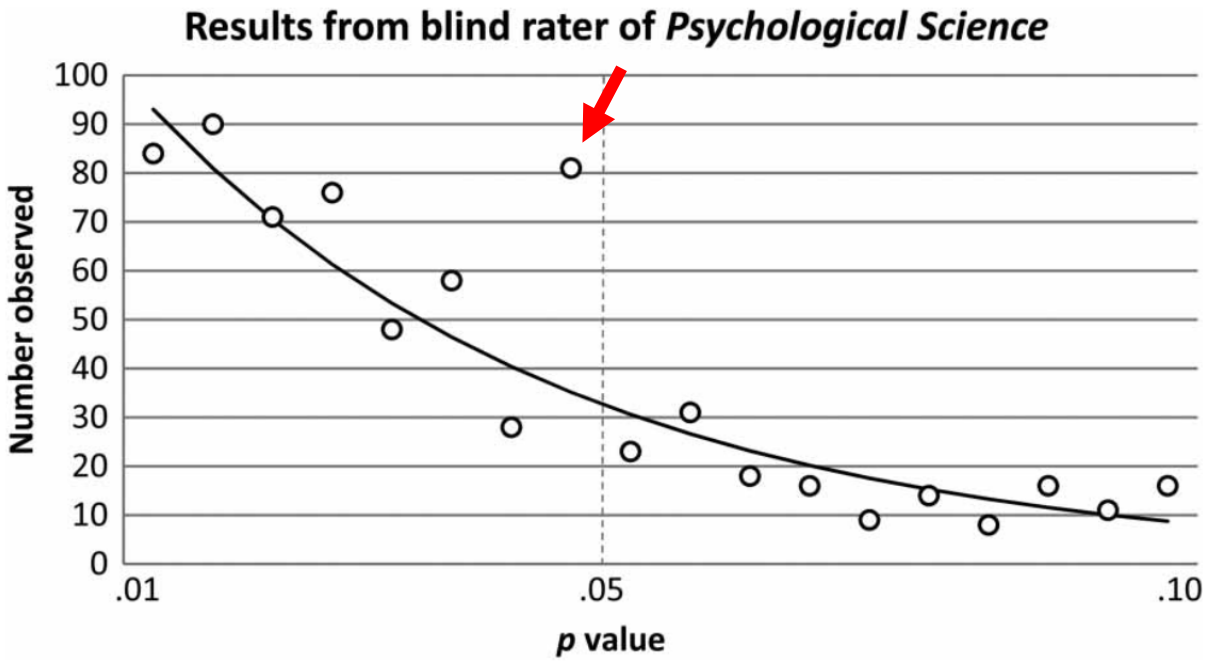


Dumas-Mallet *et al.*, *R Soc Open Sci* 2017; 4: 160254

Publication Bias and P-Hacking



P-hacking: Selectively reporting analyses that show statistically significant results and ignoring those that are non-significant*

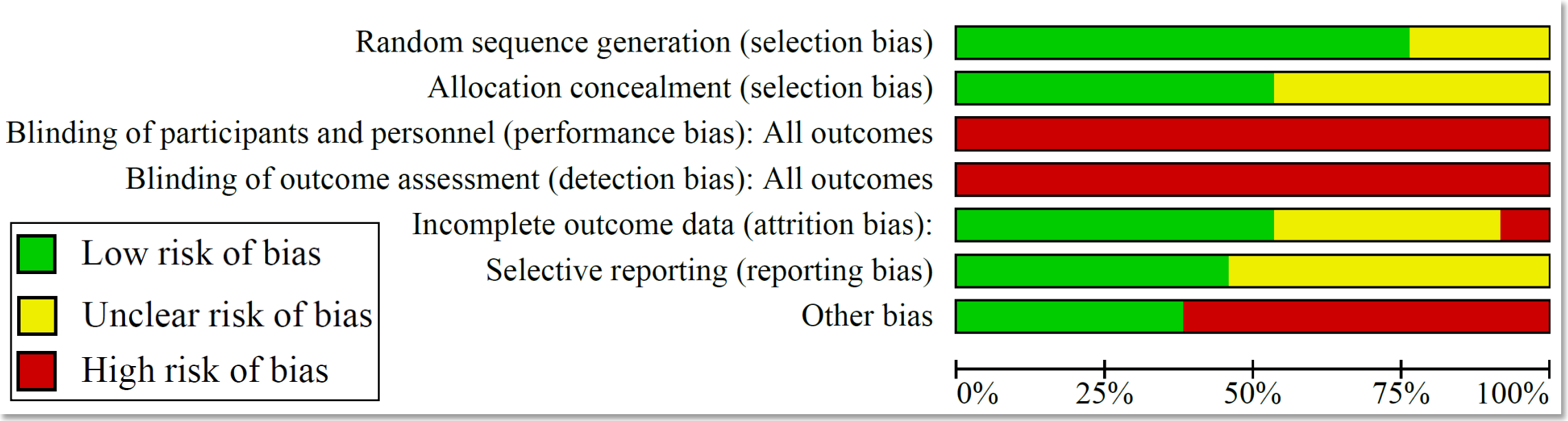


Masicampo *et al., Quar J Expt Psych* 2012; 65: 2271

NIH

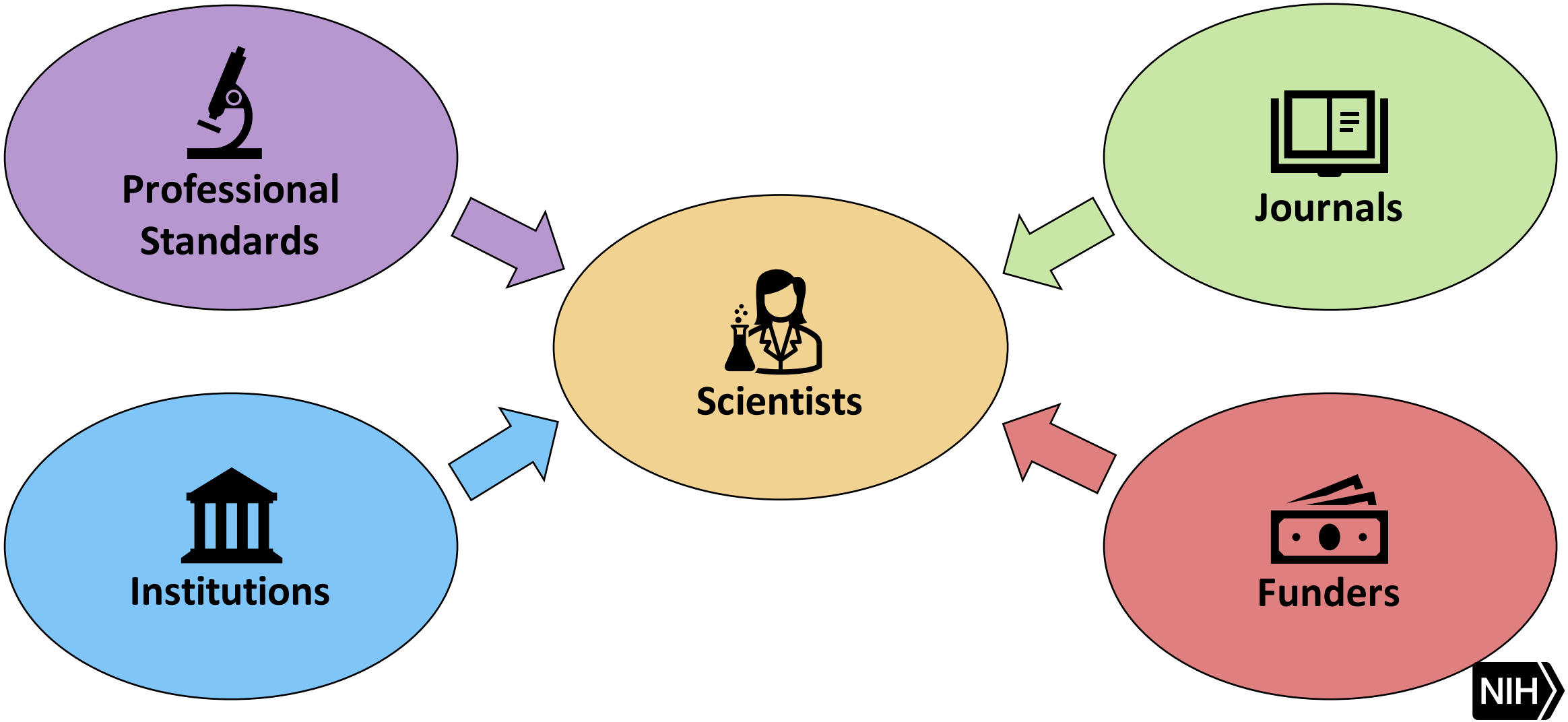
Cochrane Review: Ketogenic Diets in Drug-Resistant Epilepsy

"[W]e detected *significant risk of bias* across *all included studies*. This was largely due to a lack of blinding and unclear methodological reporting."

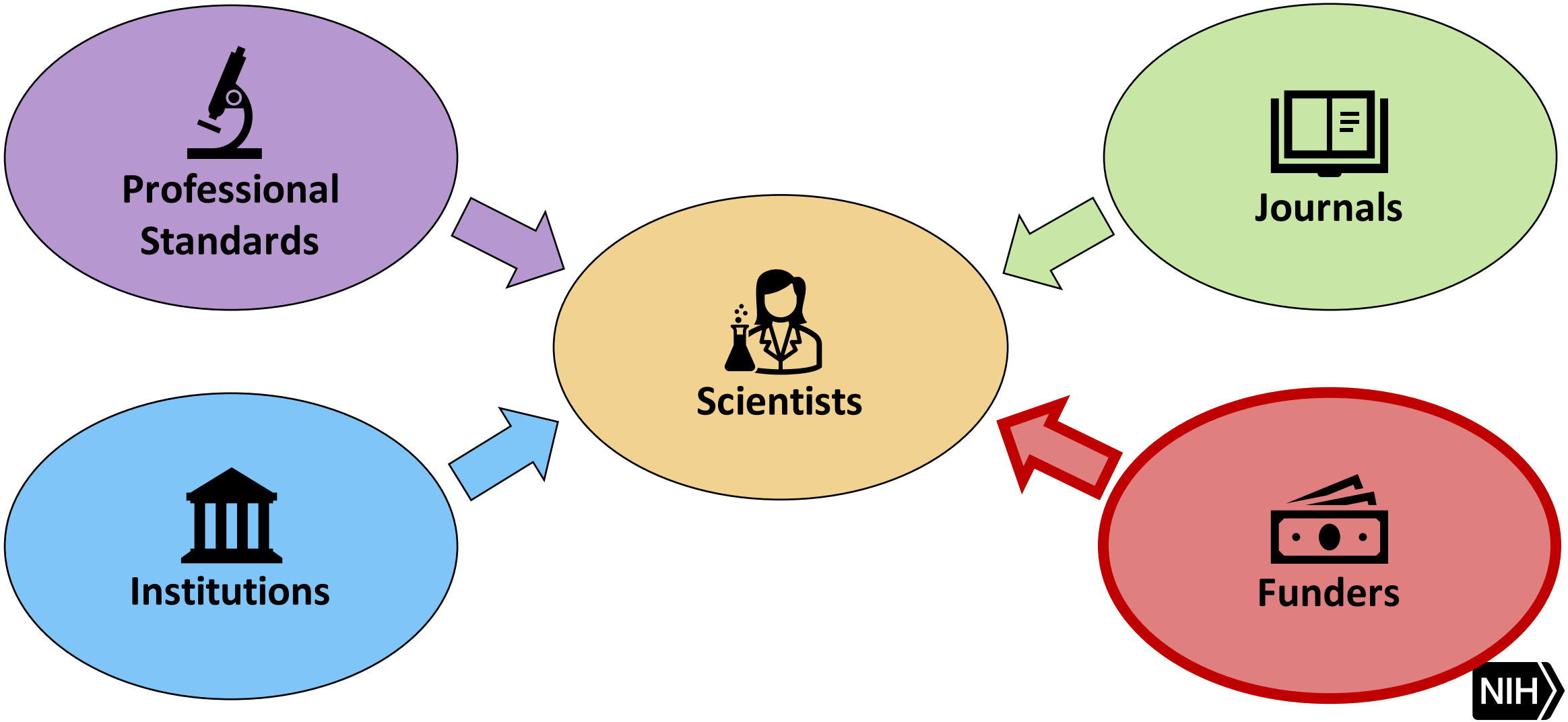


Martin-McGill *et al.*, *Cochrane Database of Systematic Rev* 2020; 6: CD001903

Scientists Experience Competing Pressures



Scientists Experience Competing Pressures



National Institute of Neurological Disorders and Stroke (NINDS)

The mission of NINDS is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease for all people.

To support this mission, NINDS:

- Supports and performs *basic, translational, and clinical neuroscience research* through grants-in-aid, contracts, scientific meetings, and through research in its own laboratories, and clinics.
- Funds and conducts *research training and career development* programs to increase basic, translational and clinical neuroscience expertise and ensure a vibrant, talented, and diverse work force.
- Promotes the timely *dissemination of scientific discoveries* and their implications for neurological health to the public, health professionals, researchers, and policy-makers.

https://www.ninds.nih.gov/About-NINDS/Who-We-Are/Mission

Spinal Cord Injury (SCI)

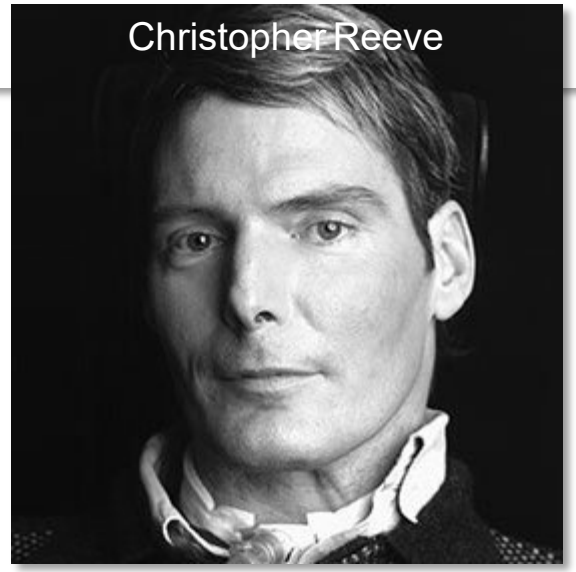
Home » Disorders » All Disorders

Spinal Cord Injury Information Page

What research is being done?

Scientists at the National Institute of Neurological Disorders and Stroke (NINDS) and those at other institutes at the National Institutes of Health (NIH) conduct and fund research to better understand SCI and how to treat it. Current research ...

See More About Research



Prognosis

Retention of movement depends on the type of injury and where it occurs along the spine. Loss of nerve function occurs below the level of injury. An injury higher on the spinal cord can cause paralysis in most of the body and affect all limbs (called tetraplegia or quadriplegia). A lower injury to the spinal cord may cause paralysis affecting the legs and lower body (called paraplegia).

People who survive a spinal cord injury will most likely have medical complications such as chronic pain and bladder and bowel dysfunction, along with an increased susceptibility to respiratory and heart problems. Successful recovery depends upon how well these chronic conditions are handled day to day.

https://www.ninds.nih.gov/Disorders/All-Disorders/Spinal-Cord-Injury-Information-Page

NINDS Preclinical Spinal Cord Injury Replication Studies

FACILITIES OF RESEARCH IN SPINAL CORD INJURY

Release Date: March 6, 2002

NOTICE: NOT-NS-02-011

RFP AVAILABLE: BAA/RFP-NIH-NINDS-02-09

National Institute of Neurological Disorders and Stroke (NINDS)
(http://www.ninds.nih.gov)

The National Institute of Neurological
Institutes of Health, announces the ava
Announcement/Request for Proposals (BA
research facilities that would support
cord injury (SCI). The NINDS is the le

Facilities of Research Excellence (FORE) in Spinal Cord Injury (SCI) Replication Studies - Request for Proposals (RFP NIH-NINDS-08-02)

Notice Number: NOT-NS-08-012

Key Dates
Release Date: December 17, 2007

Issued by
National Institute of Neurological Disorders and Stroke (NINDS) (http://www.ninds.nih.gov/)

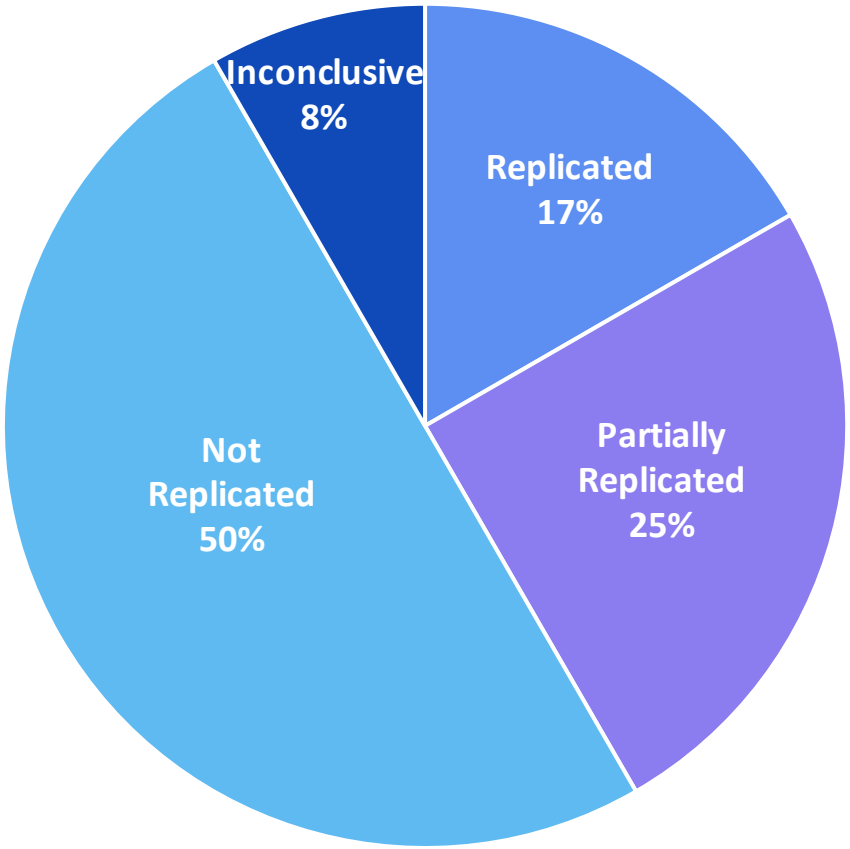
The National Institute of Neurological Disorders and Stroke (NINDS) is considering issuing contracts to identify two NINDS "Facility of Research Excellence in Spinal Cord Injury" (FORE-SCI) sites to conduct research to replicate promising studies that could lead to new and effective treatments for spinal cord injury (SCI).

https://grants.nih.gov/grants/guide/notice-files/NOT-NS-02-011.html
https://grants.nih.gov/grants/guide/notice-files/NOT-NS-08-012.html

NINDS Preclinical Spinal Cord Injury Replication Studies

Table 1
Summary of FORE-SCI replication studies.

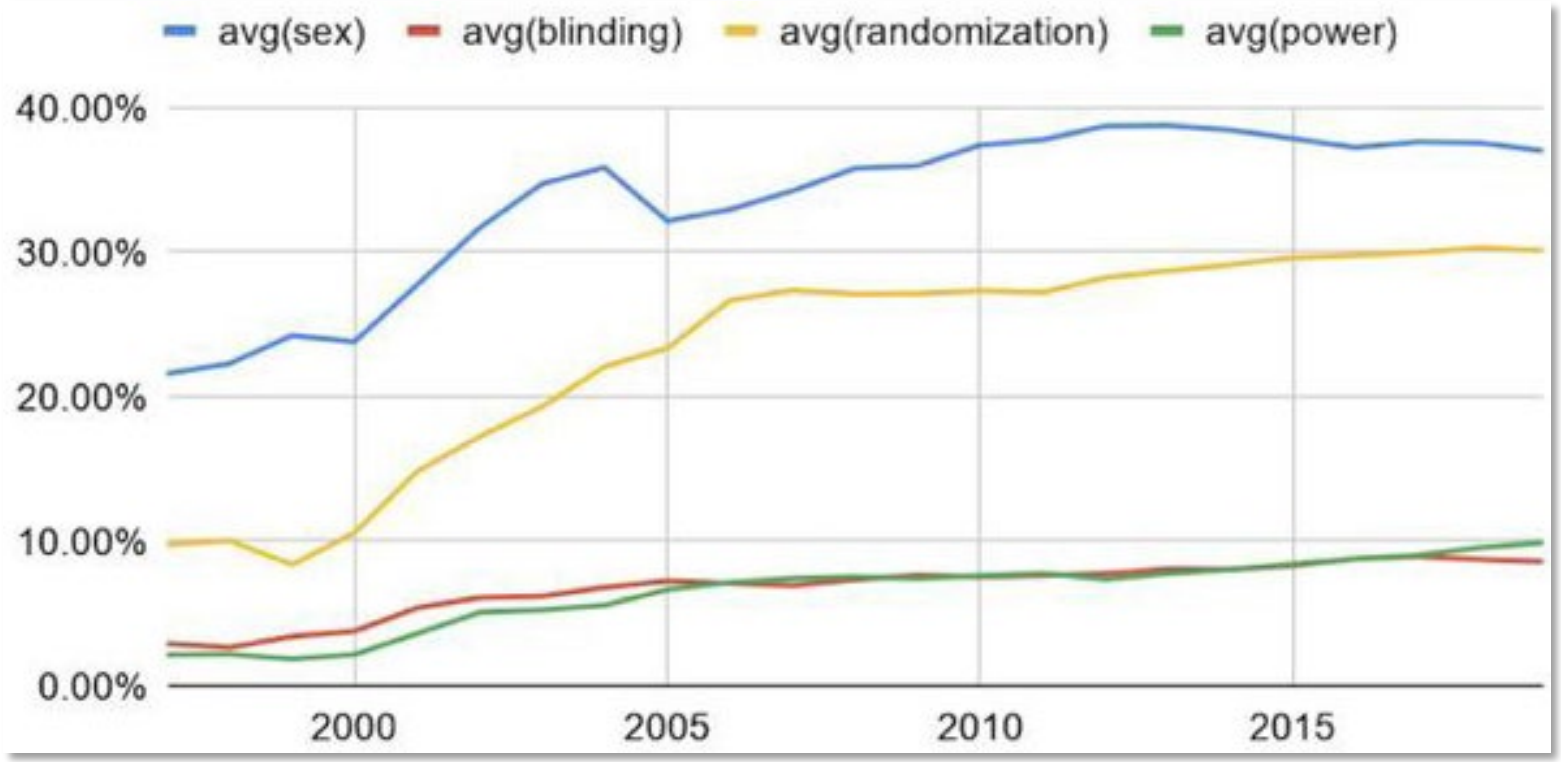
Original article	Original finding	Result of replication
Lu et al., 2002	Delayed transplant of olfactory lamina propria (OLP) improved hindlimb motor function after complete transections in rats.	No replication. No significant improvement in hindlimb function in rats that received OLP transplants.
Li and Strittmatter, 2003	Intraspinal delivery of NEP1–40 improves hindlimb motor function and enhances CST sprouting after thoracic dorsal hemisection in mice.	Partial replication. Enhancement of locomotor function in one of two duplicate studies; no difference in CST axon growth.
Pearse et al., 2004	Combined treatment with Schwann cell transplants, Rolipram and intraspinal injection of dbCAMP improves locomotor recovery after thoracic contusion in rats.	Mixed results. Rats that received Schwann cells only improved, but the combinatorial treatment was not significantly better than single treatments.
Erschbamer et al., 2007	Intraspinal delivery of an EGF receptor antagonist (PD168393) enhances recovery of hindlimb motor and bladder function after thoracic contusion in rats.	No replication. Treated group was significantly more impaired and lesion size was larger.
Bradbury et al., 2002	Intraspinal delivery of ChASE allows regeneration of CST axons following cervical dorsal crush injuries in rats.	Inconclusive because lesions spared CST in some rats. Not repeated because of other studies supporting original study.
Gorio et al., 2002	Delivery of recombinant Human Erythropoietin (EPO) reduced injury severity and improved locomotor recovery after thoracic contusion and compression in rats.	No replication. No significant effect of treatment.
Lee et al., 2004	Minocycline treatment reduces cell death and improves hindlimb motor function after contusion injury.	No replication. No significant effect of treatment.
Gris et al., 2004	Treatment with a monoclonal antibody to the CD11d integrin subunit reduced infiltration of neutrophils, improved neurological outcomes, reduced neuropathic pain and histopathological damage following clip compression injury in rats.	Partial replication. There was a trend for greater recovery and reduced tissue damage, but differences were not statistically significant.
Wang et al., 2004, Peng et al., 2009	Intraspinal delivery of P2X7 receptor blockers or systemic administration of the P2X7 receptor antagonist Brilliant Blue G improved hindlimb locomotor function and reduced injury severity after thoracic contusion in rats.	No replication. Treated groups did not differ significantly from controls.
Simard et al., 2007	Delivery of glibenclamide, which targets (SUR1)- regulated cation channels, attenuates secondary intraspinal hemorrhage and neurodegeneration following cervical hemi-contusion injury in rats.	Successfully replicated after discovering that the effect depended on the exact mechanism of injury.
Guth et al., 1994	Acute treatment with a combination of pregnenolone, LPS, and indomethacin enhanced hindlimb locomotor function and reduced lesion size after thoracic crush injury in rats.	Replicated but with less robust effects. Differences in outcomes assessment, drug composition and injury model may have degraded robustness of effect.
Benowitz et al., 1999	Intracranial delivery of inosine triggers trans-midline sprouting of CST axons after unilateral injury of the medullary pyramid in rats.	No replication. No evidence of trans-midline growth of CST axons in inosine-treated rats.



Steward *et al.*, *Exp Neurol* 2012; 233: 597

Many Publications are Not Transparent

Percentage of papers addressing reporting criteria



← Randomization

← Sample Size Estimation
← Blinding

Menke *et al.*, *iScience* 2020; 23: 101698

Amyotrophic Lateral Sclerosis (ALS)

National Institute of Neurological Disorders and Stroke

DISORDERS | FUNDING | CURRENT RESEARCH | NEWS & EVENTS | ABOUT NINDS

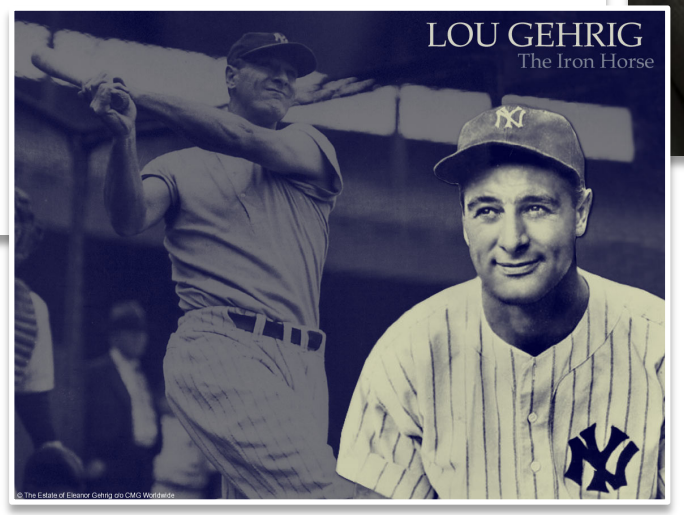
Amyotrophic Lateral Sclerosis (ALS) Information Page

Home » Disorders » All Disorders

What research is being done?

NINDS researchers hope to understand the mechanisms that trigger motor neurons to degenerate in ALS, and to find effective approaches to halt the progression leading to cell death. Different models of the disease are helping scientists study gen...

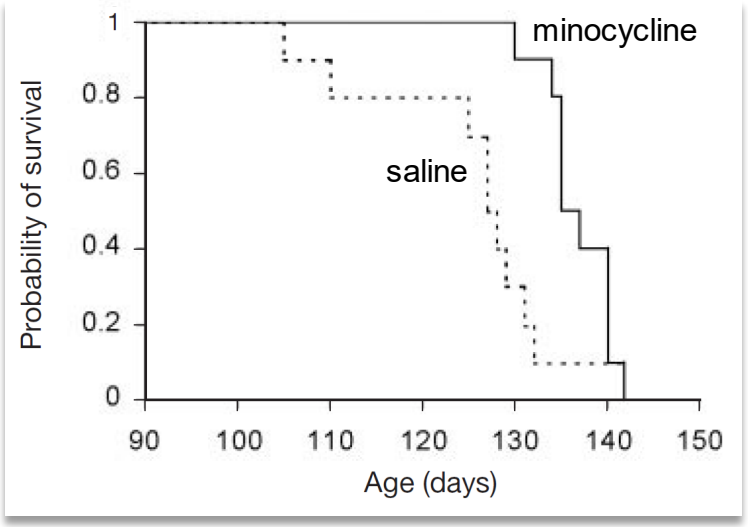
See More About Research

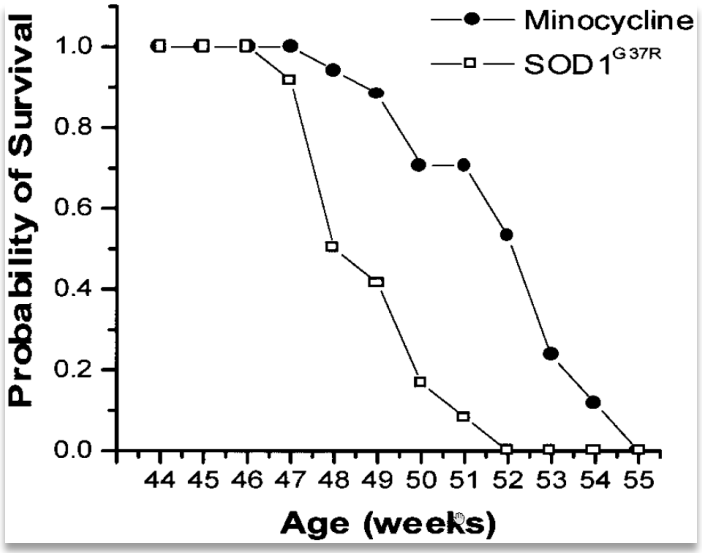


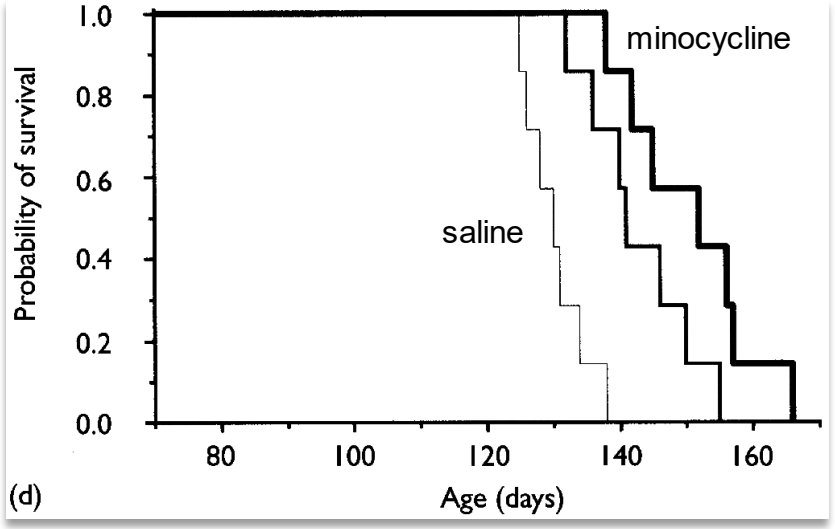
https://www.ninds.nih.gov/Disorders/All-Disorders/Amyotrophic-Lateral-Sclerosis-ALS-Information-Page

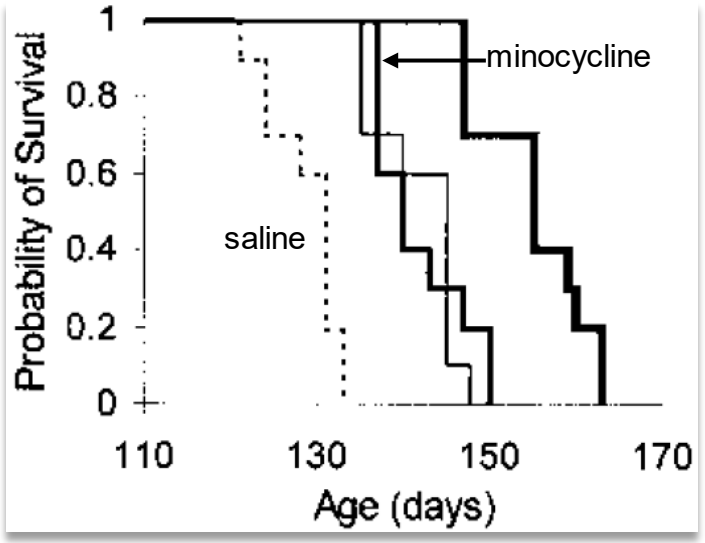
Promising Early Animal Studies of Minocycline

SOD1 transgenic mouse model:





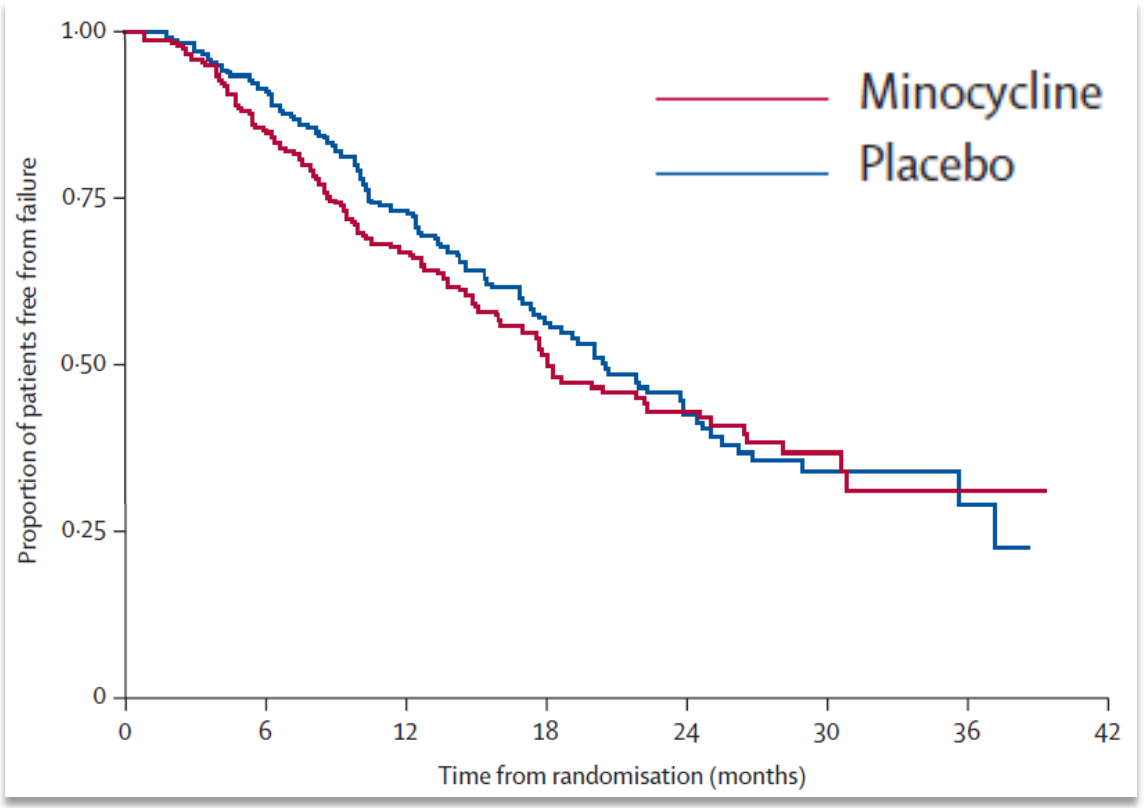




Zhu *et al.*, *Nature* 2002; 417: 74
Kriz *et al.*, *Neurobiol Dis* 2002; 10: 268
Van Den Bosch *et al.*, *NeuroReport* 2002; 13: 1067
Zhang *et al.*, *Annals of Neurol* 2003; 53: 267

Randomized, Placebo-Controlled Trial of Minocycline

Multi-center, placebo-controlled trial with 412 patients:

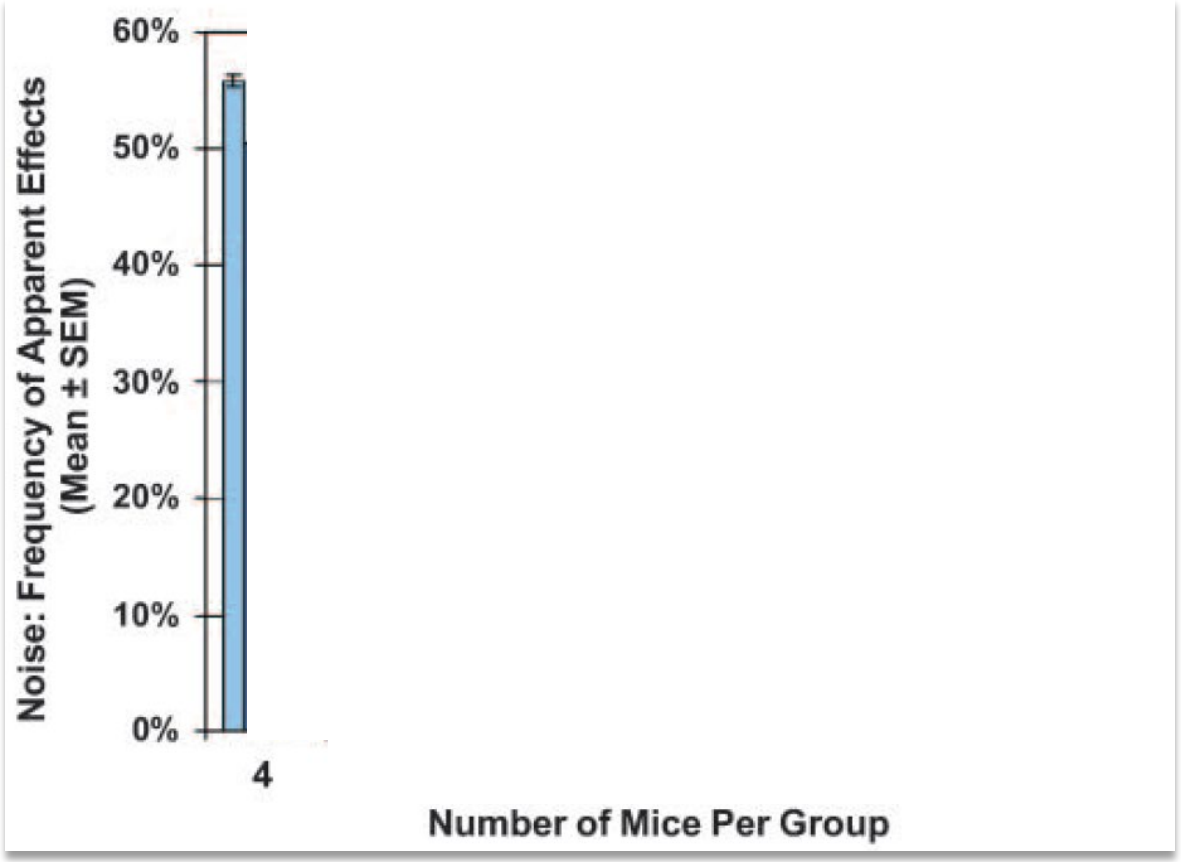


Gordon *et al.*, *Lancet Neurol* 2007; 6: 1045

ALS Therapy Development Institute Compiled Prior Studies

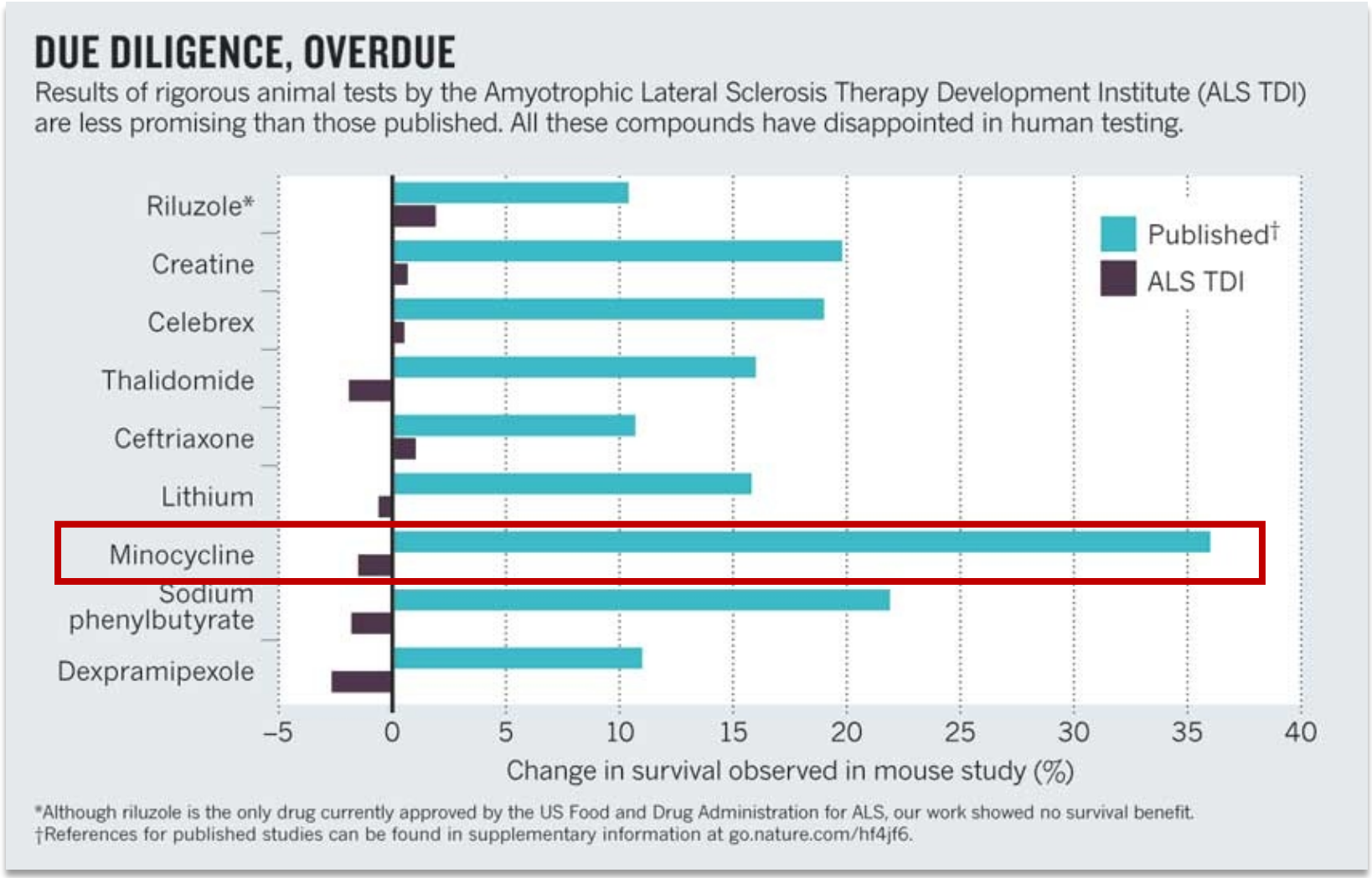
- Thousands of simulations on 2241 control animals (untreated SOD1 transgenic mice)

- **Largest confounders:**
  - Low copy number transgenic mice
  - Non-ALS-related deaths (e.g. infection)
  - Lack of sex and litter matching
  - Low sample size



Scott *et al.*, *Amyotroph Lateral Scler* 2009; 9: 4

ALS Therapy Development Institute's "Optimized" Studies



Perrin, *Nature* 2014; 507: 423

NINDS Led the Charge for Improved Rigor at NIH

Improving the Quality of NINDS-Supported Preclinical and Clinical Research through Rigorous Study Design and Transparent Reporting

Notice Number: NOT-NS-11-023

Key Dates

Release Date: August 10, 2011

NINDS believes that applications that propose preclinical research, or that are based on previous preclinical data, will be greatly strengthened if the design, execution, and interpretation of the proposed studies and supporting data are adequately described. NINDS encourages investigators, whenever possible, to address these elements directly in their applications.

Shai Silberberg

Afterward, NINDS Clinical Trial applications subjected to two-part discussion during review:

1) How rigorous were the preclinical experiments that justify the clinical trial?
2) How rigorous are the proposed experiments?

https://grants.nih.gov/grants/guide/notice-files/NOT-NS-11-023.html

NINDS Workshop and "Landis 4" Paper

- Investigators
- Reviewers
- Journal Editors
- Funders

PERSPECTIVE

doi:10.1038/nature11556

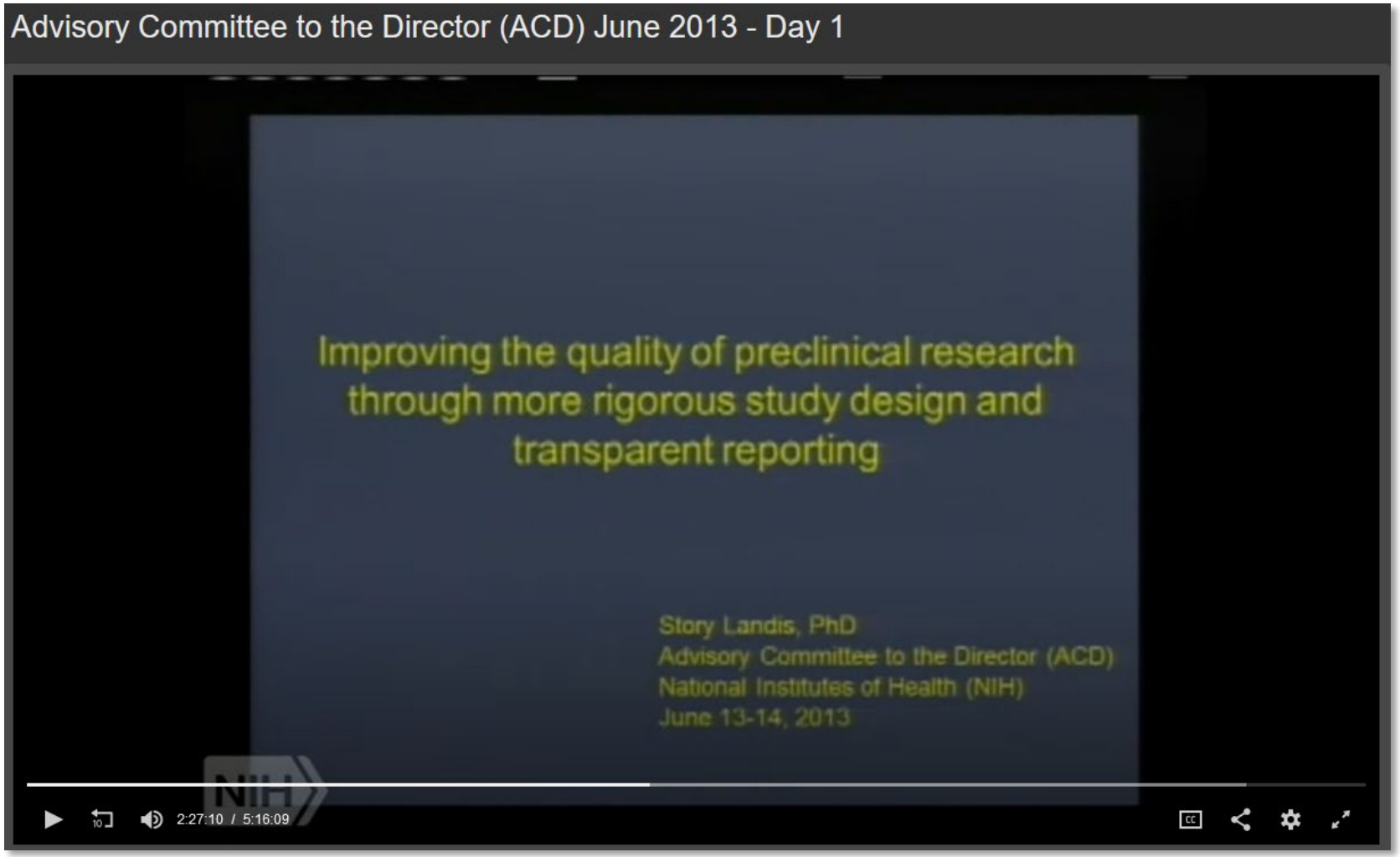
A call for transparent reporting to optimize the predictive value of preclinical research

Story C. Landis[1], Susan G. Amara[2], Khusru Asadullah[3], Chris P. Austin[4], Robi Blumenstein[5], Eileen W. Bradley[6], Ronald G. Crystal[7], Robert B. Darnell[8], Robert J. Ferrante[9], Howard Fillit[10], Robert Finkelstein[1], Marc Fisher[11], Howard E. Gendelman[12], Robert M. Golub[13], John L. Goudreau[14], Robert A. Gross[15], Amelie K. Gubitz[1], Sharon E. Hesterlee[16], David W. Howells[17], John Huguenard[18], Katrina Kelner[19], Walter Koroshetz[1], Dimitri Krainc[20], Stanley E. Lazic[21], Michael S. Levine[22], Malcolm R. Macleod[23], John M. McCall[24], Richard T. Moxley III[25], Kalyani Narasimhan[26], Linda J. Noble[27], Steve Perrin[28], John D. Porter[1], Oswald Steward[29], Ellis Unger[30], Ursula Utz[1] & Shai D. Silberberg[1]

1. **Blinding**
2. **Randomization**
3. **Sample size estimation**
4. **Data handling**

Landis *et al.*, *Nature* 2012; 490: 187

NINDS Presentation to the NIH ACD



Story Landis

https://videocast.nih.gov/summary.asp?live=12741

NIH Committed to Improving Rigor

NIH plans to enhance reproducibility

Francis S. Collins and **Lawrence A. Tabak** discuss initiatives that the US National Institutes of Health is exploring to restore the self-correcting nature of preclinical research.

A growing chorus of concern, from scientists and laypeople, contends that the complex system for ensuring the reproducibility of biomedical research is failing and is in need of restructuring[1,2]. As leaders of the US National Institutes of Health (NIH), we share this concern and here explore some of the significant interventions that we are planning.

Science has long been regarded as 'self-correcting', given that it is founded on the replication of prior work. Over the long term, that principle remains true. In the shorter term, however, the checks and balances that once ensured scientific fidelity have been hobbled. This has compromised the ability of today's researchers to reproduce others' findings.

Let's be clear: with rare exceptions, we have no evidence to suggest that irreproducibility is about scientific misconduct. In 2011, the Office of Research Integrity of the US Department of Health and Human Services pursued only 12 such cases[3]. Even if this represents only a fraction of the actual problem, such papers are vastly

- Training
- Grant applications
- Raw data

"Efforts by the NIH alone will not be sufficient to effect real change in this unhealthy environment."

Collins & Tabak, *Nature* 2014; 505: 612

NIH Notified the Community of Upcoming Changes

Enhancing Reproducibility through Rigor and Transparency

Notice Number: NOT-OD-15-103

Key Dates

Release Date: June 9, 2015

"Newly revised grant application instructions will: *clarify long-standing expectations* to ensure that NIH is funding the best and most rigorous science; highlight the need for applicants to *describe details that may have been previously overlooked*; highlight the need for *reviewers to consider such details in their reviews* through revised review criteria; and minimize additional burden."

NIH National Institutes of Health
Office of Extramural Research

extramural NEXUS

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Scientific Rigor in NIH Grant Applications

By Mike Lauer

Posted January 28, 2016

Share | Tweet | 9 Comments

In part two of our series on rigor and transparency in research grant and career development award applications, we focus on scientific rigor, the strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation, and reporting of results.

We can all agree that attention to scientific rigor is important. But how can we be sure a rigorous experiment was performed? In published papers, full transparency in reporting experimental details is crucial for others to assess, reproduce, and extend the findings. Likewise, in grant applications, full transparency is necessary for reviewers to properly assess the proposed studies.

Therefore, as part of the Approach section of the Research Strategy, updated instructions clarify this expectation to emphasize how the experimental design and methods proposed will achieve robust and unbiased results. Solid, well-controlled experiments can produce robust results capable of being reproduced under well-controlled conditions using reported experimental details. A robust approach might include use of appropriate statistical methods, prospective sample size estimation, replicates, or standards (for example, reference reagents or data standards). Robust and credible results are those obtained with methods specifically designed to avoid bias, such as blinding, randomization, and prospectively defined exclusion/inclusion criteria, to name a few.

https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-103.html
https://nexus.od.nih.gov/all/2016/01/28/scientific-rigor-in-nih-grant-applications/

NIH Implemented New Application Guidance in 2016

Implementing Rigor and Transparency in NIH & AHRQ Research Grant Applications

Notice Number: NOT-OD-16-011

Key Dates

Release Date: October 9, 2015

Updates include:

- Revisions to application guide instructions for preparing your research strategy attachment
- Use of a new "Authentication of Key Biological and/or Chemical Resources" attachment
- Additional rigor and transparency questions reviewers will be asked to consider when reviewing applications

These updates focus on four areas deemed important for enhancing rigor and transparency:

https://grants.nih.gov/grants/guide/notice-files/not-od-16-011.html

"Scientific Premise"

"The **scientific premise** for an application is the research that is used to form the basis for the proposed research question; NIH has always strived to fund projects that are based on a strong foundation. Moving forward, NIH expects applicants to describe the general strengths and weaknesses of the prior research *being cited by the investigator* as crucial to support the application."

2017 NINDS analysis:

- Many investigators and reviewers misunderstood "scientific premise" to mean general rationale

https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-103.html

NIH Updated Application Guidelines in 2019

NIH & AHRQ Announce Upcoming Updates to Application Instructions and Review Criteria for Research Grant Applications

Notice Number: NOT-OD-18-228

Key Dates

Release Date: September 14, 2018

Summary of Updates

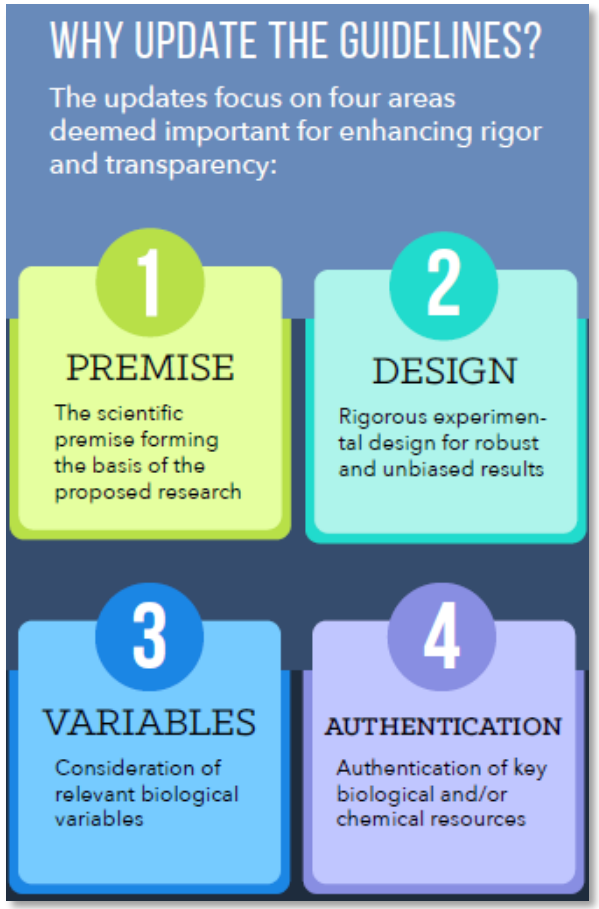
Revisions to the application guide will be available through the How to Apply - Application Guide websit

Form	Section	Heading	Current language	Revised language
Research Plan	Research Strategy	Significance	Describe the scientific premise for the proposed project, including consideration of the strengths and weaknesses of published research or preliminary data crucial to the support of your application.	Describe the strengths and weaknesses in the rigor of the prior research (both published and unpublished) that serves as the key support for the proposed project.
Research Plan	Research Strategy	Approach	Not Applicable	Describe plans to address weaknesses in the rigor of the prior research that serves as the key support for the proposed project.

https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-228.html

2019 Update Summary

2016



2019

https://grants.nih.gov/reproducibility/documents/grant-guideline.pdf

Current Guidelines: Rigor of the Prior Research

1) Describe the **strengths and weaknesses in the rigor of the prior research** (both published and unpublished) that serves as the *key support for the proposed project* and plans to address these weaknesses.

The rigor of the prior research

- A careful assessment of the **rigor of the prior research** that serves as the key support for a proposed project helps to identify weakness or gaps in a line of research. NIH expects applicants to describe the general strengths and weaknesses in the rigor of the prior research (both published and unpublished) that serves as the key support for the proposed project. It is expected that this consideration includes attention to the rigor of the previous experimental designs, as well as the incorporation of relevant biological variables and authentication of key resources. Applicants are expected to include plans to address any weaknesses or gaps identified.

https://grants.nih.gov/policy/reproducibility/guidance.htm

Current Guidelines: Rigor of the Proposed Research

2) Scientific rigor is the strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation and reporting of results. *This includes full transparency in reporting experimental details* so that others may reproduce and extend the findings.

What is meant by "robust" and "unbiased"?

Robust results are obtained using methods designed to avoid bias and can be reproduced under well-controlled and reported experimental conditions. Applicants should consider methods to reduce bias, such as having multiple individuals recording assessments, defining terminology in advance, using independent, blinded assessors, etc.

https://grants.nih.gov/faqs#/rigor-and-reproducibility.htm?anchor=question54415

Current Guidelines: Biological Variables

3) Biological variables, such as sex, age, weight, and underlying health conditions, are often critical factors affecting health or disease. NIH expects that sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies.

Which relevant biological variables do we need to consider?

Applicants should consider the biological variables that are relevant to the experimental design of the study. The choice of animal model or human population to be included will vary with the scientific topic of the proposed research. For example, sex, age, weight, and underlying health conditions are biological variables often affecting health or disease and should be considered where applicable.

https://grants.nih.gov/faqs#/rigor-and-reproducibility.htm?anchor=question54416

Current Guidelines: Authentication of Key Resources

4) Key biological and/or chemical resources include, but are not limited to, cell lines, specialty chemicals, antibodies and other biologics. The quality of resources used to conduct research is critical to the ability to reproduce the results.

ATTACHMENT FOR AUTHENTICATION OF KEY BIOLOGICAL AND/OR CHEMICAL RESOURCES

You must briefly describe methods to ensure the identity and validity of key biological and/or chemical resources used in the proposed studies.

These include, but are not limited to:

CELL LINES

SPECIALTY CHEMICALS

ANTIBODIES

OTHER BIOLOGICS

Standard laboratory reagents that are not expected to vary do not need to be included in the plan. Examples are buffers and other common biologicals or chemicals.

DO NOT put experimental methods or preliminary data in this section

DO focus on authentication and validation of key resources

https://grants.nih.gov/reproducibility/documents/grant-guideline.pdf

Parallel Reviewer Questions

REVIEW GUIDELINES

Here are the additional criteria the reviewers will be asked to use:

- Is the **prior research** that serves as the key support for the proposed project **rigorous?**
- Have the investigators included plans to **address weaknesses in the rigor of prior** research that serves as the key support for the proposed project?
- Have the investigators presented **strategies to ensure a robust and unbiased approach**, as appropriate for the work proposed?
- Have the investigators presented adequate plans to address **relevant biological variables, such as sex,** for studies in vertebrate animals or human subjects?

Reviewers will also be asked to comment on that new attachment (see **Update 2**)!

https://grants.nih.gov/reproducibility/documents/grant-guideline.pdf

Always Check FOAs for Additional Instructions

NINDS Institutional Research Training Program T32 (PAR-21-149):

Research Training Program Plan Must Address:

- Experimental Design
- Statistical Methodology
- Statistical Training and Support
- Quantitative Literacy and the Use of Quantitative Approaches
- Program-Wide Meetings: Experimental Design, Statistics and Quantitative Literacy
- Scientific Rigor

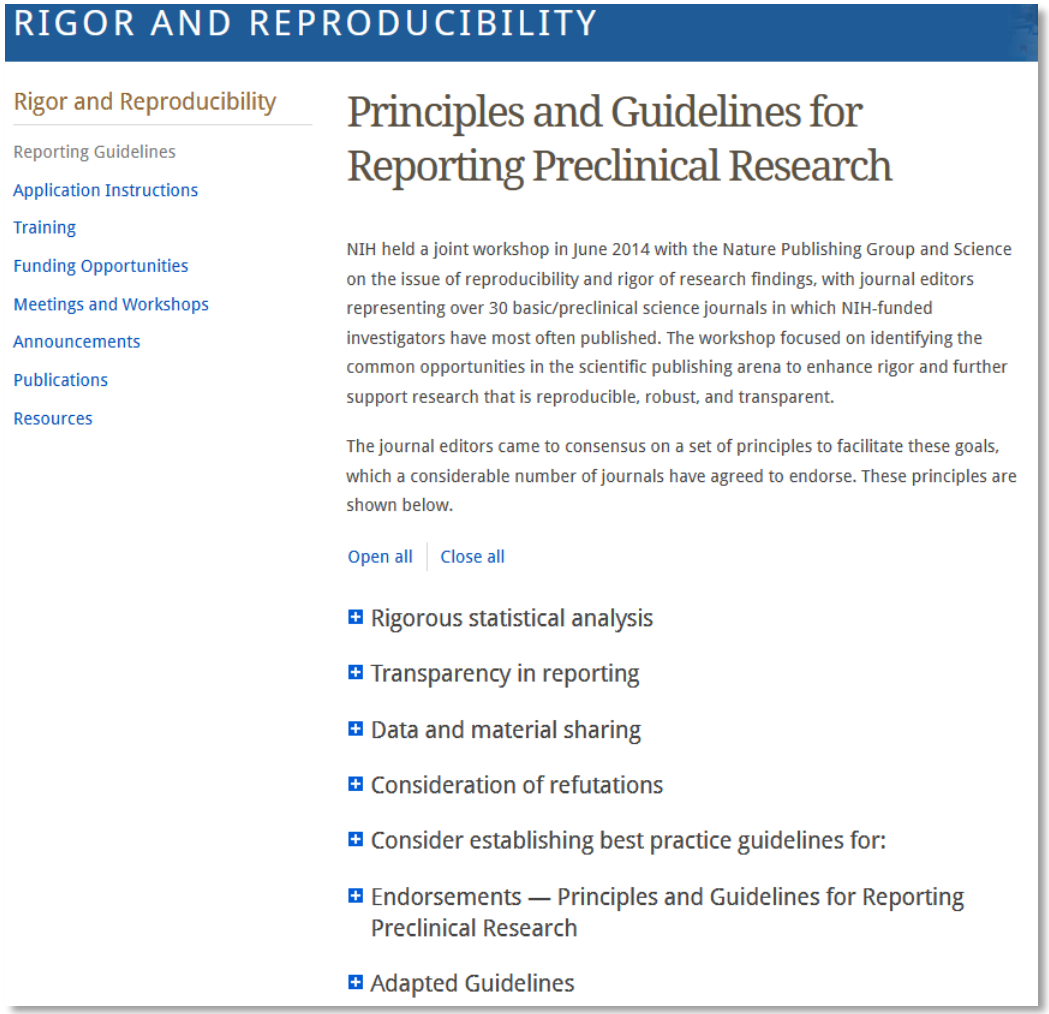
NINDS Translational Outcomes Project in Neurotrauma UG3/UH3 (RFA-NS-17-023):

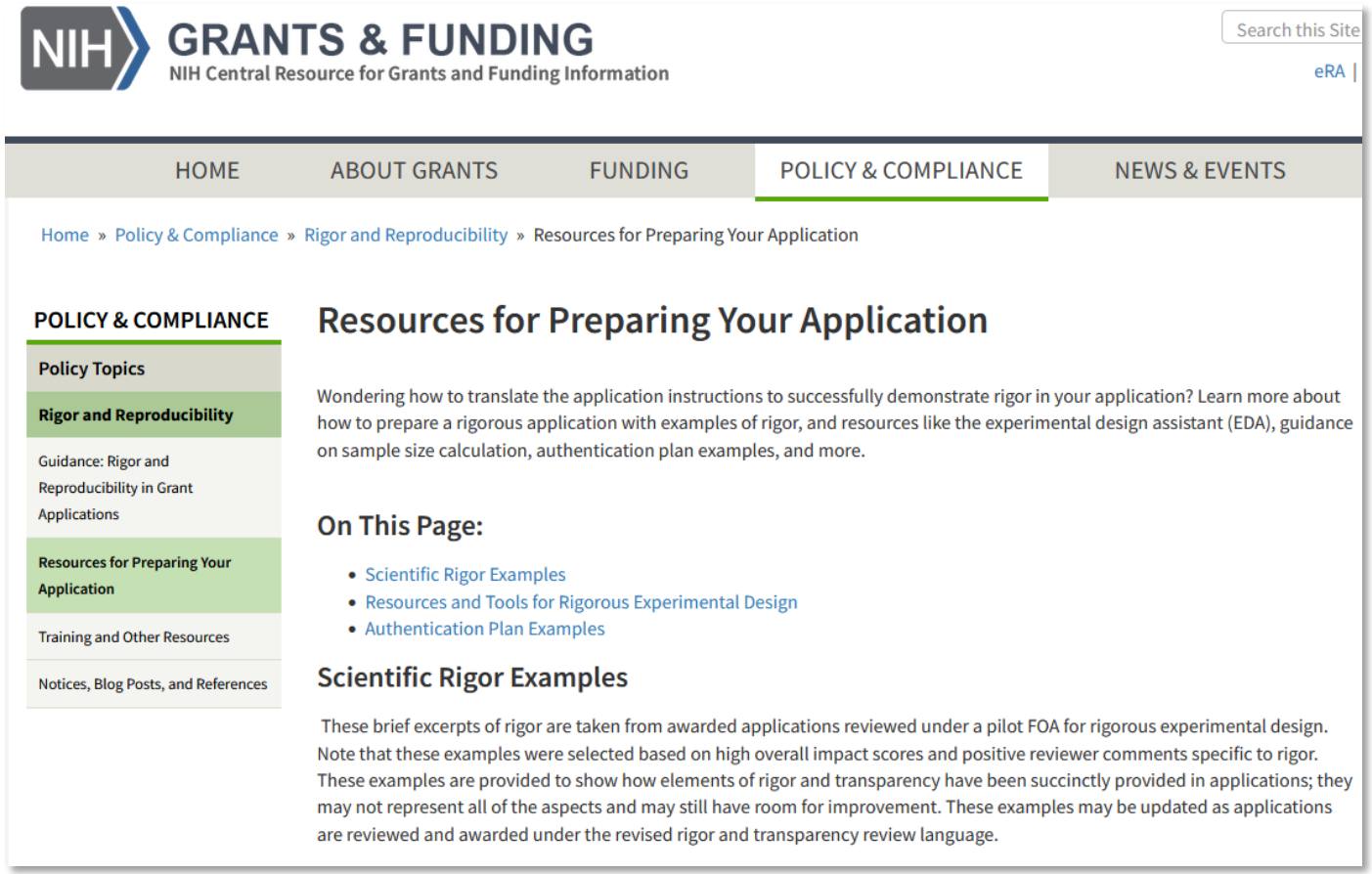
Research Plan Must Address:

- Strengths and quality of the data used to provide the basis for the chosen measures
- Feasibility, reliability and comparability to practical clinical assessments
- Key metadata to enable reproducibility
- Design and statistical approaches to establish reproducibility and test internal and external validity of outcome measures

https://grants.nih.gov/grants/guide/pa-files/PAR-21-149.html
https://grants.nih.gov/grants/guide/rfa-files/rfa-ns-17-023.html

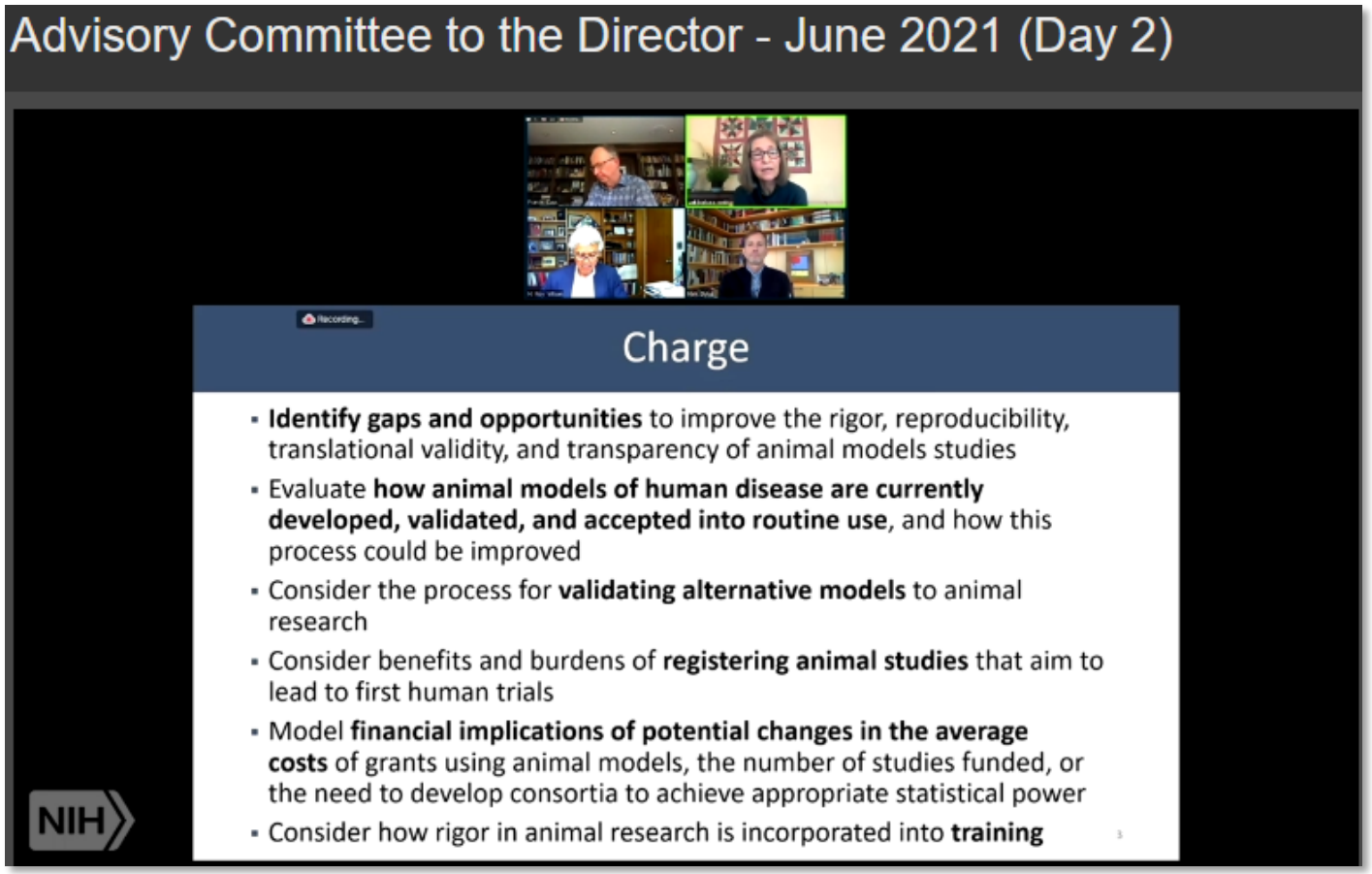
NIH Resources for Publications and Grant Applications

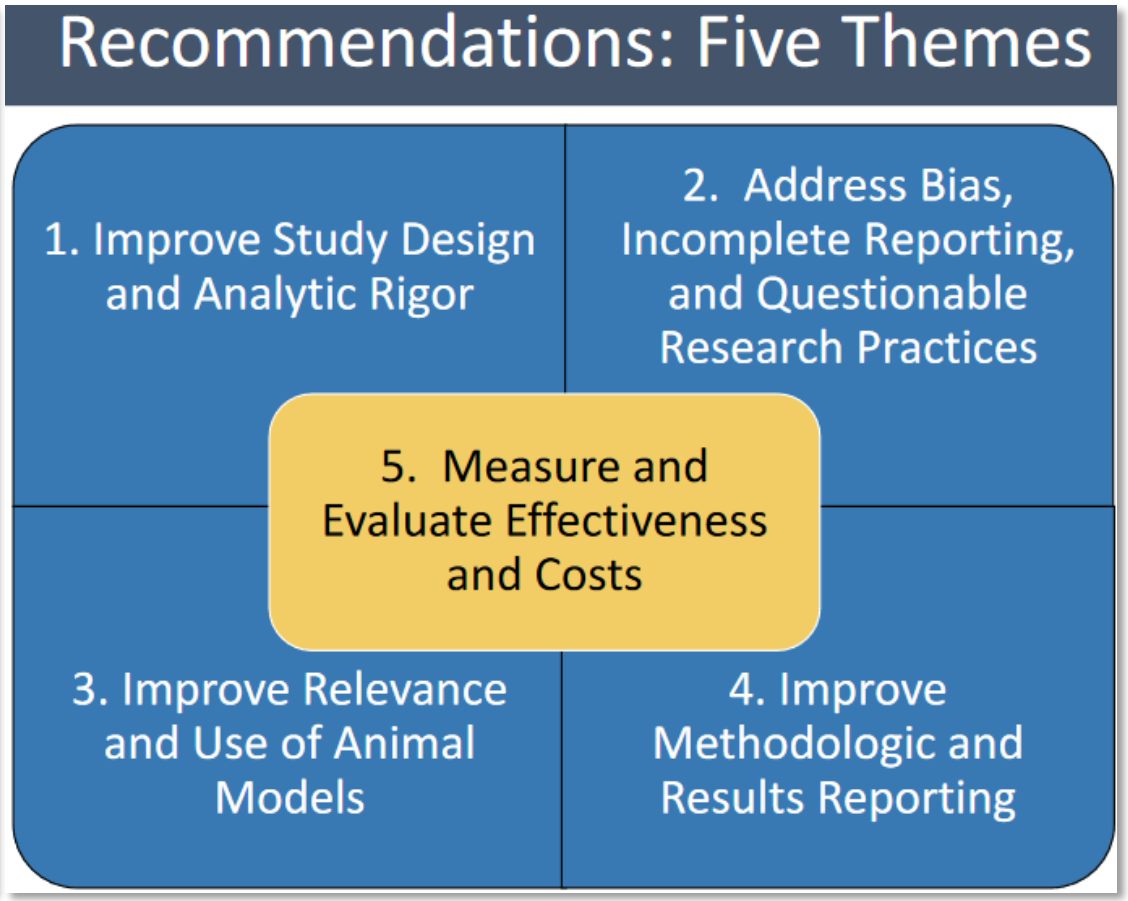




https://www.nih.gov/research-training/rigor-reproducibility/principles-guidelines-reporting-preclinical-research
https://grants.nih.gov/policy/reproducibility/resources.htm

ACD Working Group on Enhancing Rigor, Transparency, and Translatability in Animal Research





https://videocast.nih.gov/watch=42270

Upcoming NIH Policy for Data Management and Sharing

Final NIH Policy for Data Management and Sharing

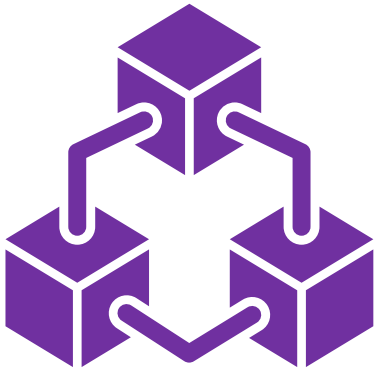
Notice Number:
NOT-OD-21-013

Key Dates

Release Date:	October 29, 2020
Effective Date:	January 25, 2023

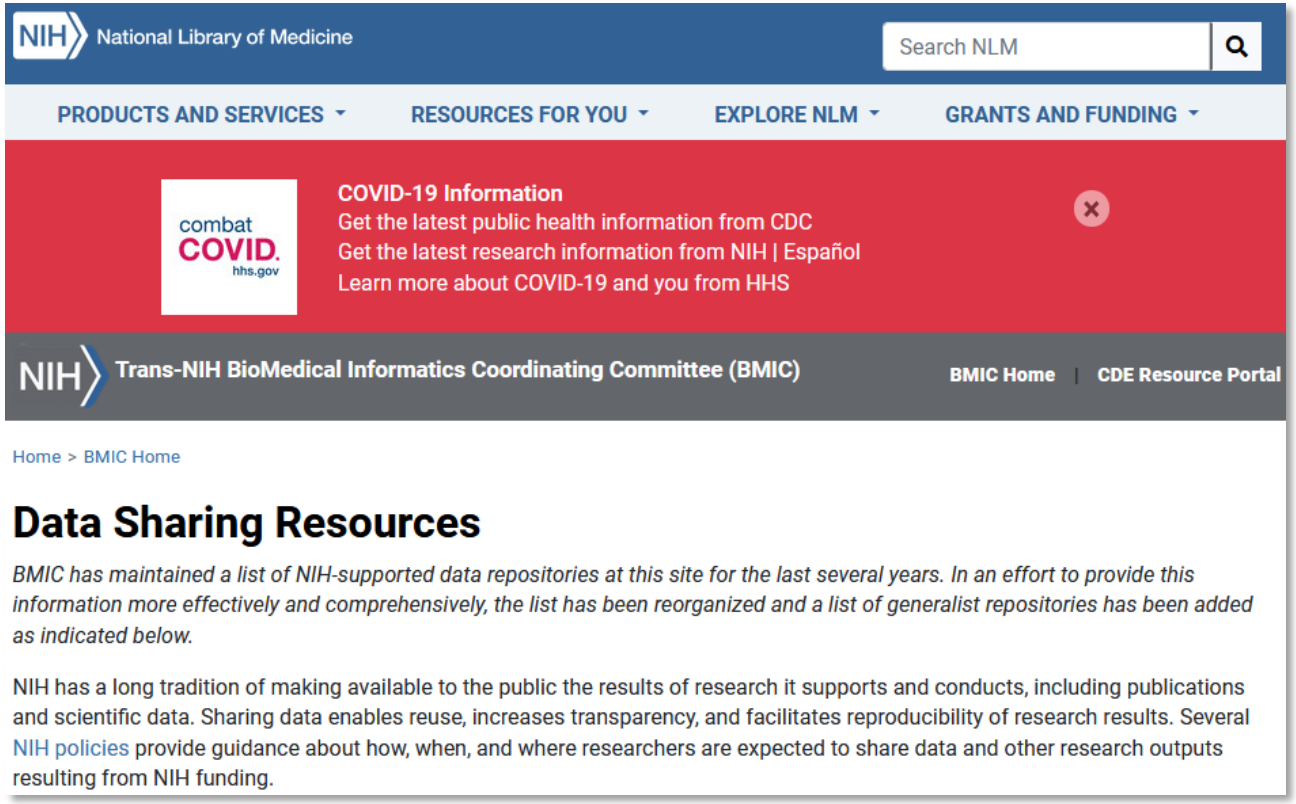
- *Budget Justification* section
- Data and accompanying *metadata* released at the *time of publication* or the *end of the award* (whichever is earlier) to *established repository*
- *Programmatic review*

"This Policy establishes the *requirements of submission of Data Management and Sharing Plans* … It also emphasizes the *importance of good data management practices* and establishes the *expectation for maximizing the appropriate sharing of scientific data* generated from NIH-funded or conducted research, with justified limitations or exceptions."



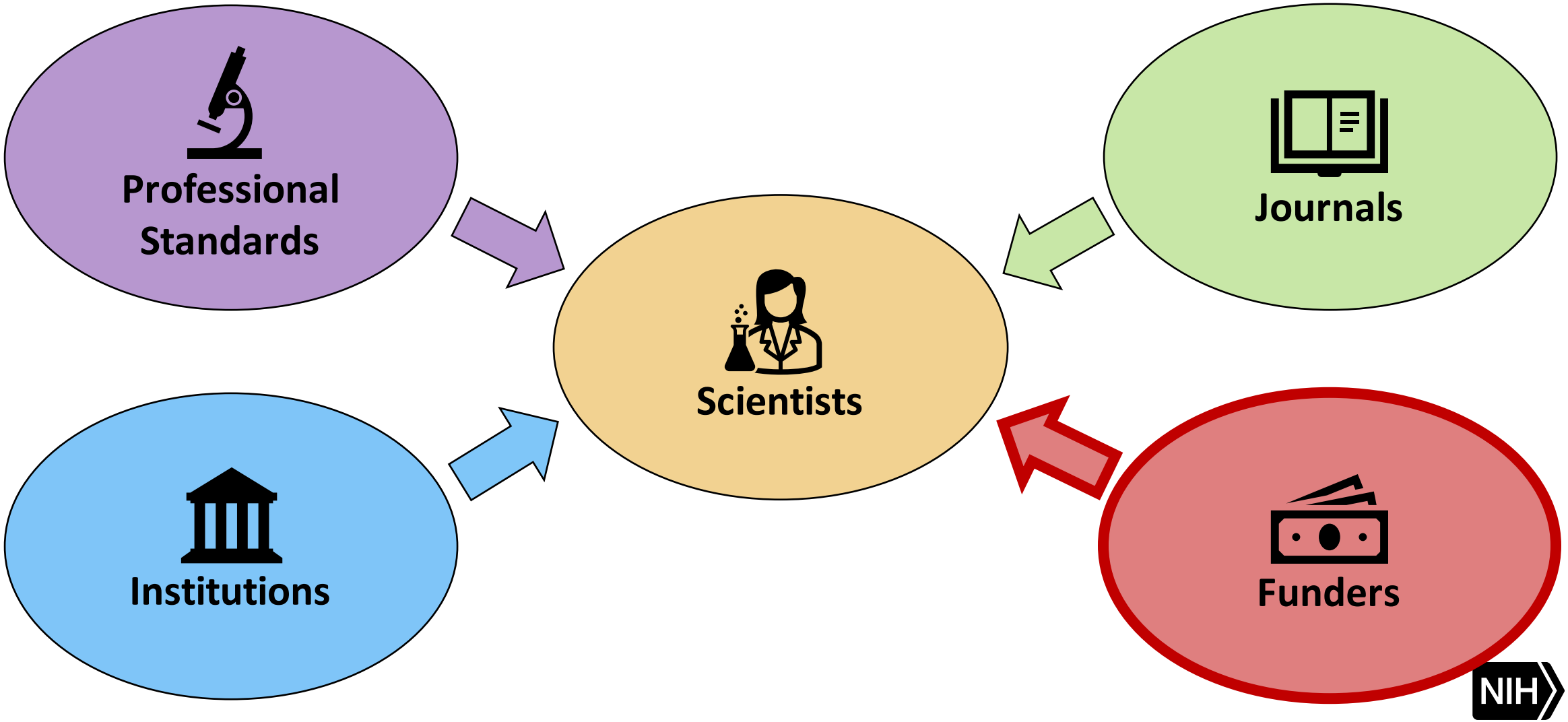
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-013.html

Data Science Resources at NIH

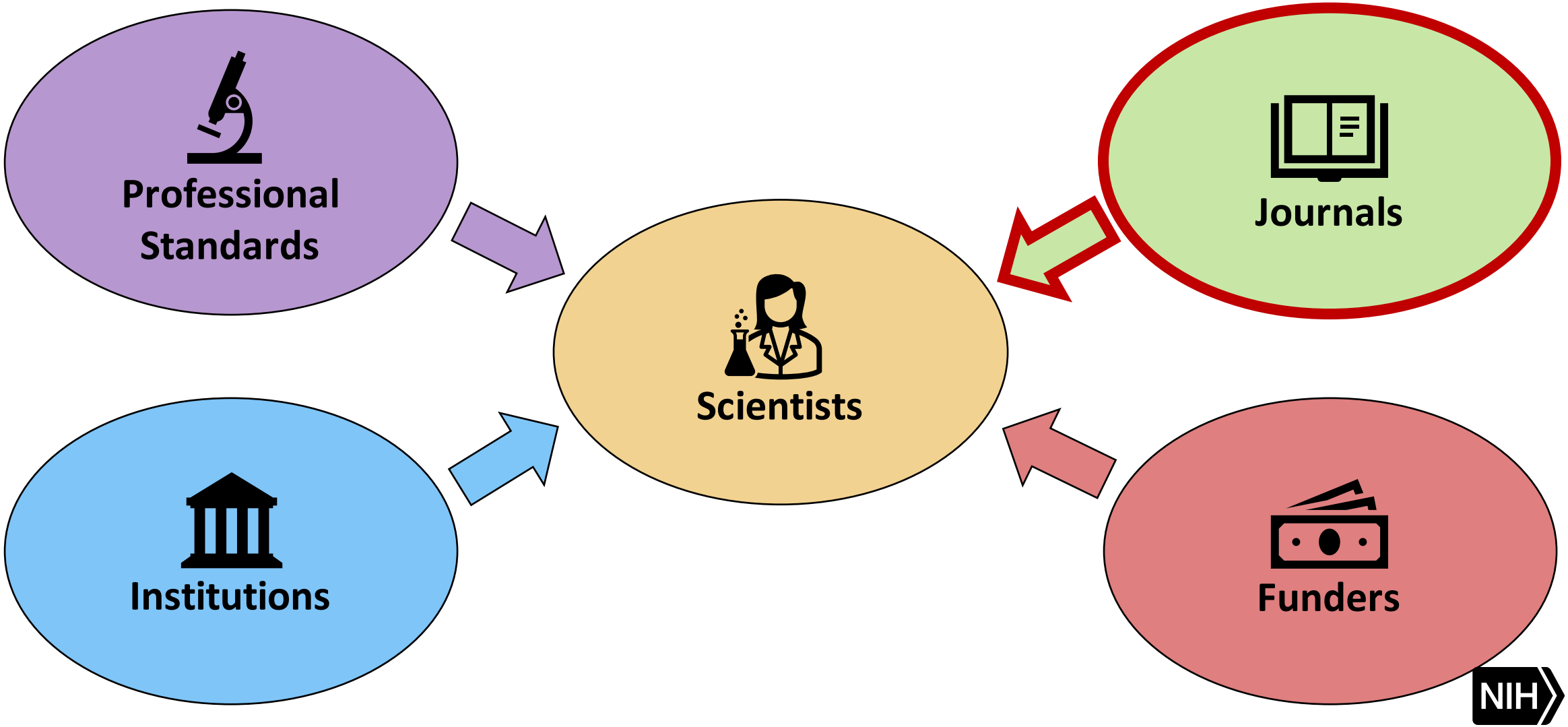


https://datascience.nih.gov/
https://www.nlm.nih.gov/NIHbmic/nih_data_sharing_repositories.html

Scientists Experience Competing Pressures



Scientists Experience Competing Pressures



Journal Checklists for Increasing Reporting Transparency

nature

ANNOUNCEMENT

Reducing our irreproducibility

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	*Describe how sample size was determined, detailing any statistical m was performed, describe how sample sizes were chosen and provide*
Data exclusions	*Describe any data exclusions. If no data were excluded from the anal rationale behind them, indicating whether exclusion criteria were pre*
Replication	*Describe the measures taken to verify the reproducibility of the exper OR if there are any findings that were not replicated or cannot be rep*
Randomization	*Describe how samples/organisms/participants were allocated into ex were controlled OR if this is not relevant to your study, explain why.*
Blinding	*Describe whether the investigators were blinded to group allocation describe why OR explain why blinding was not relevant to your study.*

Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study.
For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

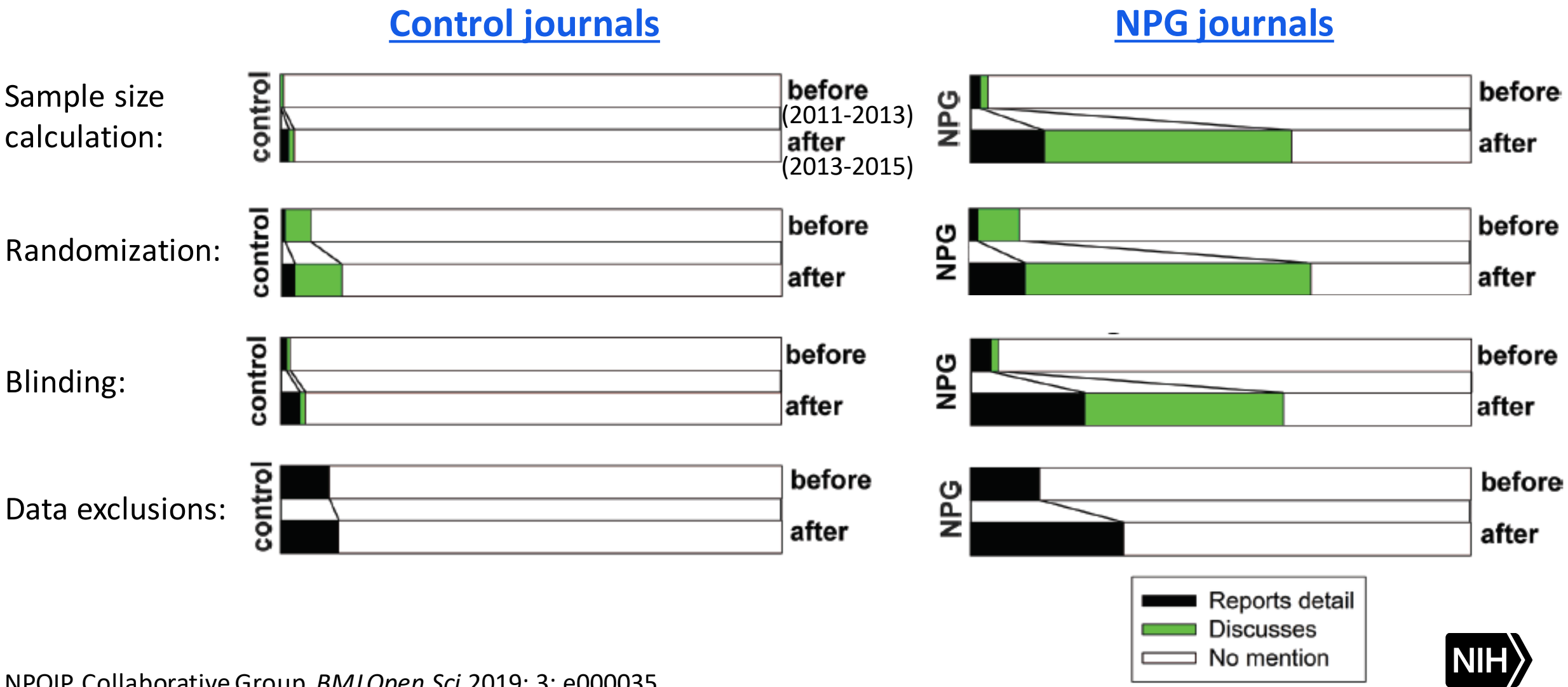
n/a	Confirmed	
☐	☐	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☐	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☐	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☐	A description of all covariates tested
☐	☐	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☐	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☐	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☐	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☐	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

NIH

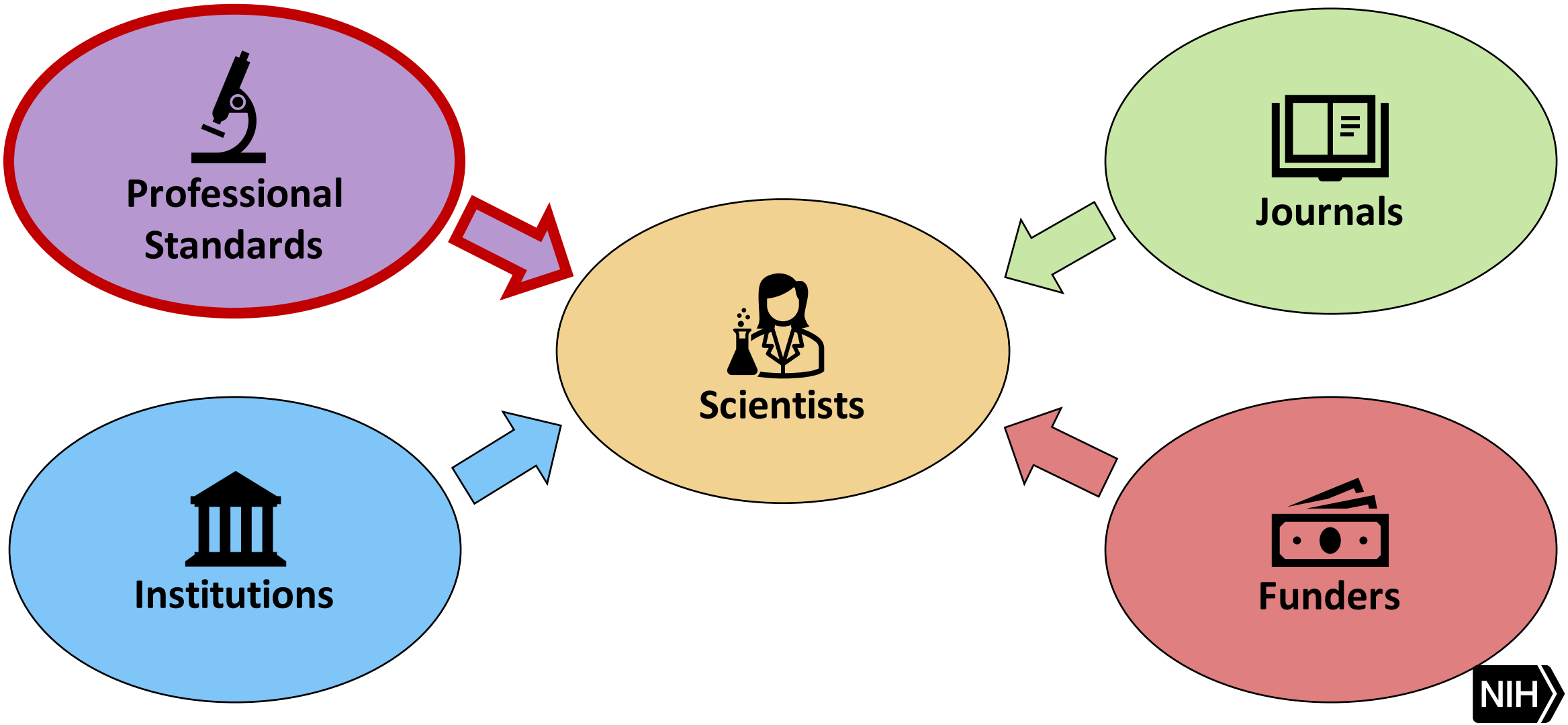
https://www.nature.com/documents/nr-reporting-summary.pdf

Journal Checklists Improve Reporting



NPQIP Collaborative Group, *BMJ Open Sci* 2019; 3: e000035

Scientists Experience Competing Pressures



Scientific Transparency at Conferences

COMMENT

EVOLUTION How mechanisms of fate and chance affect adaptation p.156 | **PALAEOBIOLOGY** Why access to samples of ancient DNA must be regulated p.158 | **TAXONOMY** Species boundaries should be defined more stably p.158 | **CRYPTOGOVERNANCE** Use the blockchain to trade energy securely p.158

EBBI ROE YOUNG-WWW.GARYWAGNERPHOTOS.COM

Poster sessions at conferences are often where early research gets its first airing.

Shake up conferences

Emojis, smartphone technologies and revamped guidelines would boost transparency at scientific meetings, say **Shai D. Silberberg** and colleagues.

than 30 small research conferences a year, collectively bringing together more than 4,000 attendees. By contrast, the annual meeting of the Society for Neuroscience regularly draws more than 28,000 people.

Conferences have served as crucial hubs for scientific communication for at least four centuries. They provide an essential platform that facilitates collaboration and disseminates information, and they enable researchers to gain feedback on early-stage work. They also train scientists and set standards for quality.

And yet the staples of scientific conferences — presentations and poster sessions — can provide only snapshots of ongoing work. This is exacerbated by the complexity of scientific technologies, richness of acquired data and sophistication of data-analysis methods, all of which are ever-growing. As a result, attendees can find it difficult to evaluate presented results and interpret the findings. This hinders their ability to give feedback to colleagues and to decide how to incorporate findings into their own work.

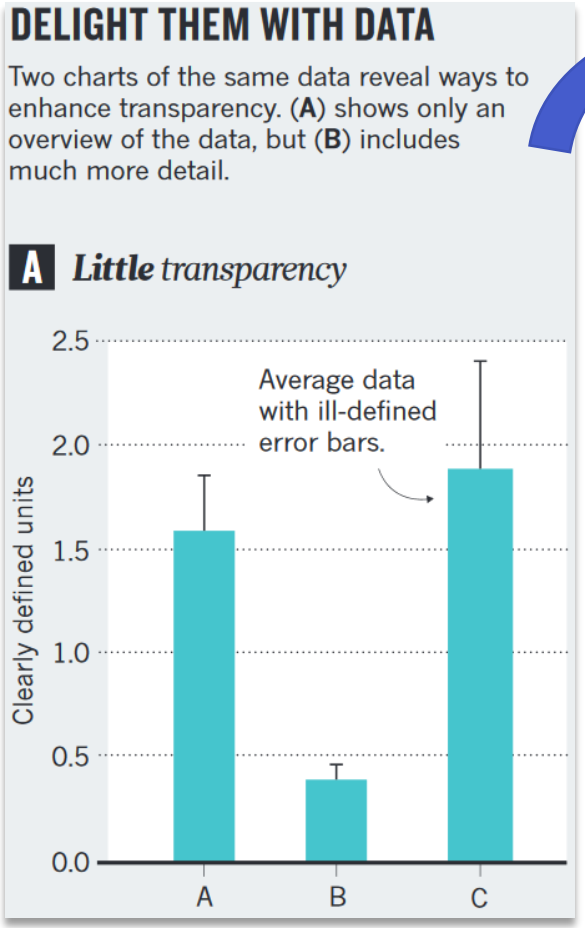
We suggest that a few straightforward strategies could yield vast improvements.

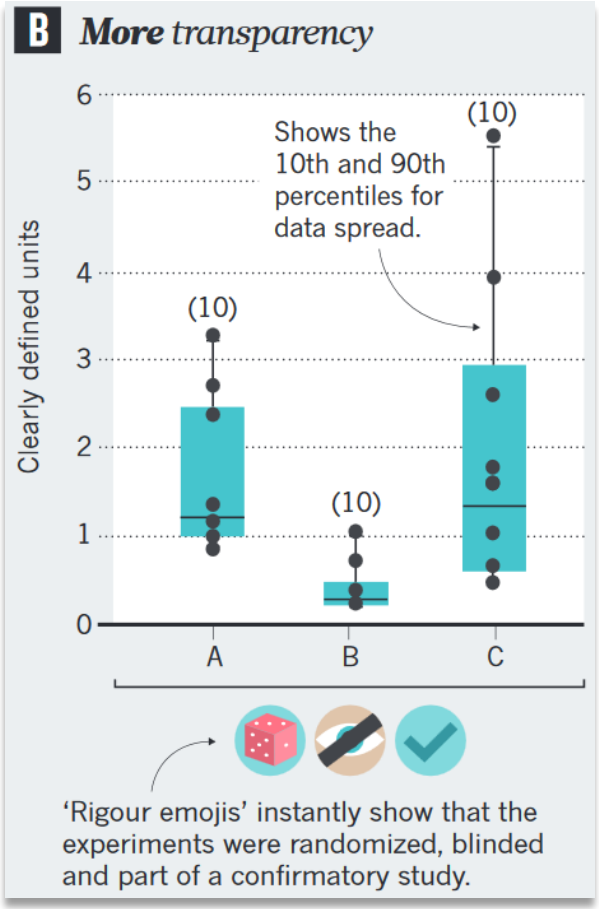
Rewrite presentation and poster guidelines to promote transparency. Instructions for conference participants focus on formats and logistics. For example, at the American Society of Clinical Oncology (ASCO) annual meeting, instructions state that slides for oral presentations must be in 16:9 widescreen format, and presenters are required to declare whether their research was federally funded. Posters must be no larger than 120 centimetres by 240 centimetres and in landscape orientation. Bold, readable fonts are encouraged.

Formatting instructions like these are important, but so are guidelines that promote transparency. Meeting participants should be encouraged to present relevant information regarding the research question and its

DELIGHT THEM WITH DATA

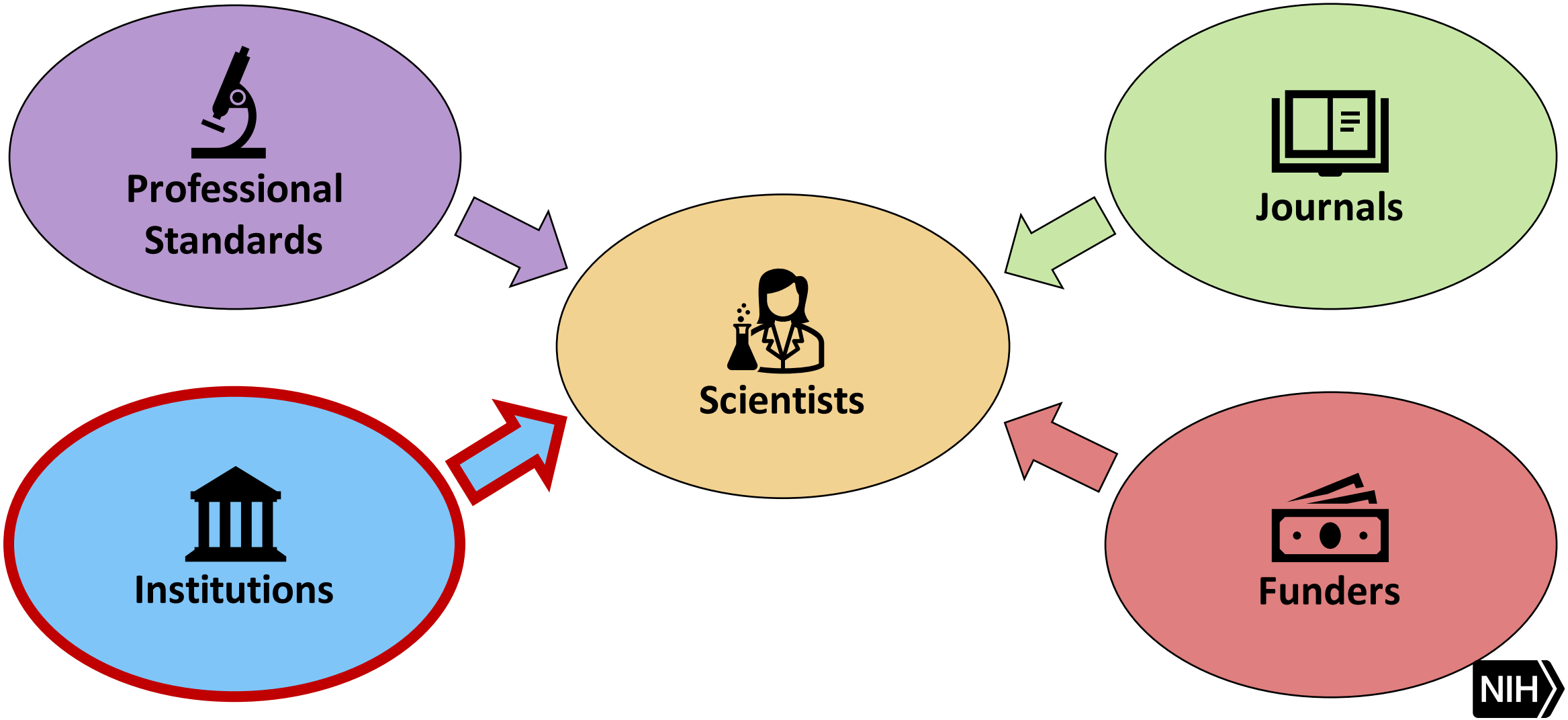
Two charts of the same data reveal ways to enhance transparency. (**A**) shows only an overview of the data, but (**B**) includes much more detail.





Silberberg *et al.*, *Nature* 2017; 548: 153

Scientists Experience Competing Pressures



Efforts to Change Hiring and Promotion/Tenure Practices

https://sfdora.org/read/

"**General Recommendation:**

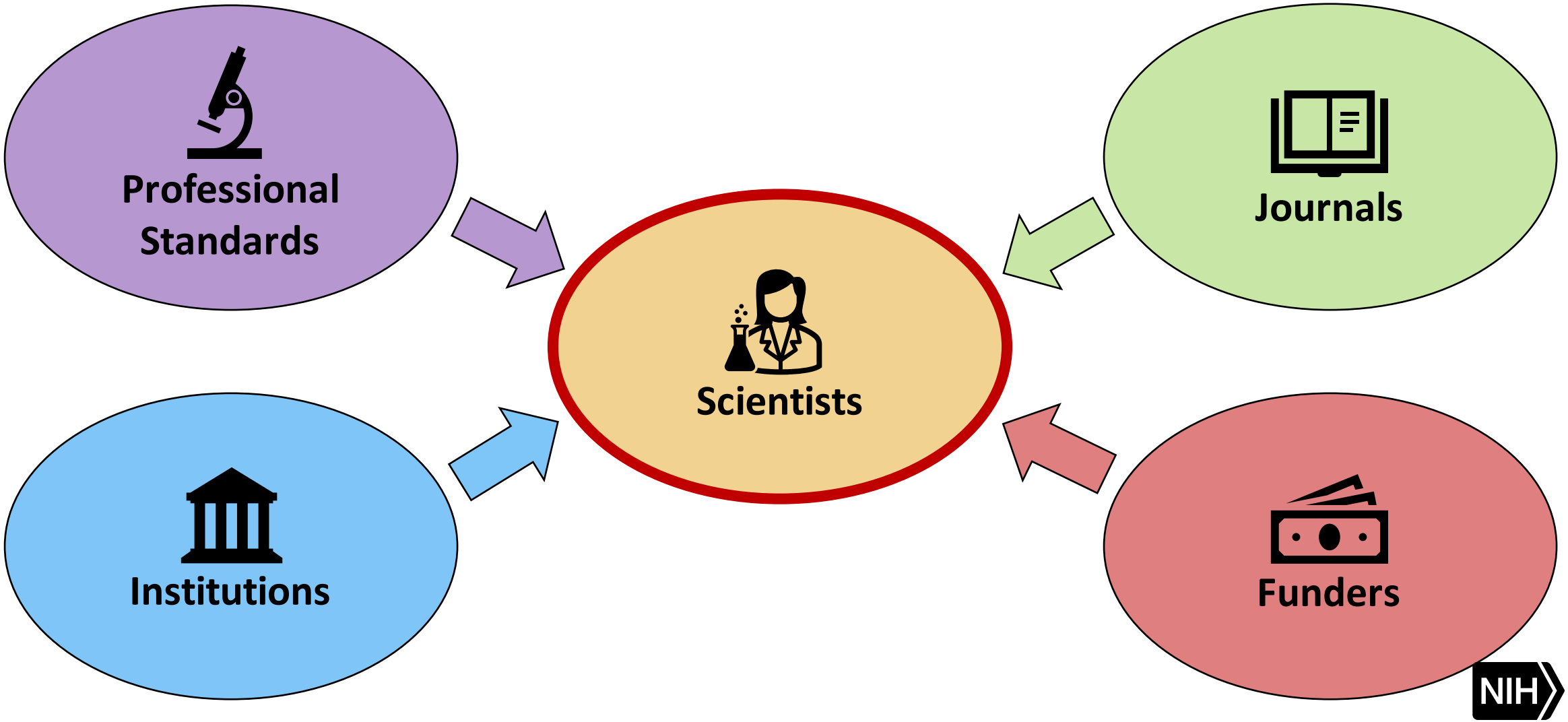
- *Do not use journal-based metrics, such as Journal Impact Factors, as a surrogate measure of the quality of individual research articles*, to assess an individual scientist's contributions, or in hiring, promotion, or funding decisions.

For institutions:

- Be explicit about the criteria used to reach hiring, tenure, and promotion decisions, clearly highlighting, especially for early-stage investigators, that *the scientific content of a paper is much more important than publication metrics or the identity of the journal* in which it was published.

- For the purposes of research assessment, consider the *value and impact of all research outputs* (including datasets and software) in addition to research publications, and consider a broad range of impact measures including qualitative indicators of research impact, such as influence on policy and practice."

Scientists Experience Competing Pressures



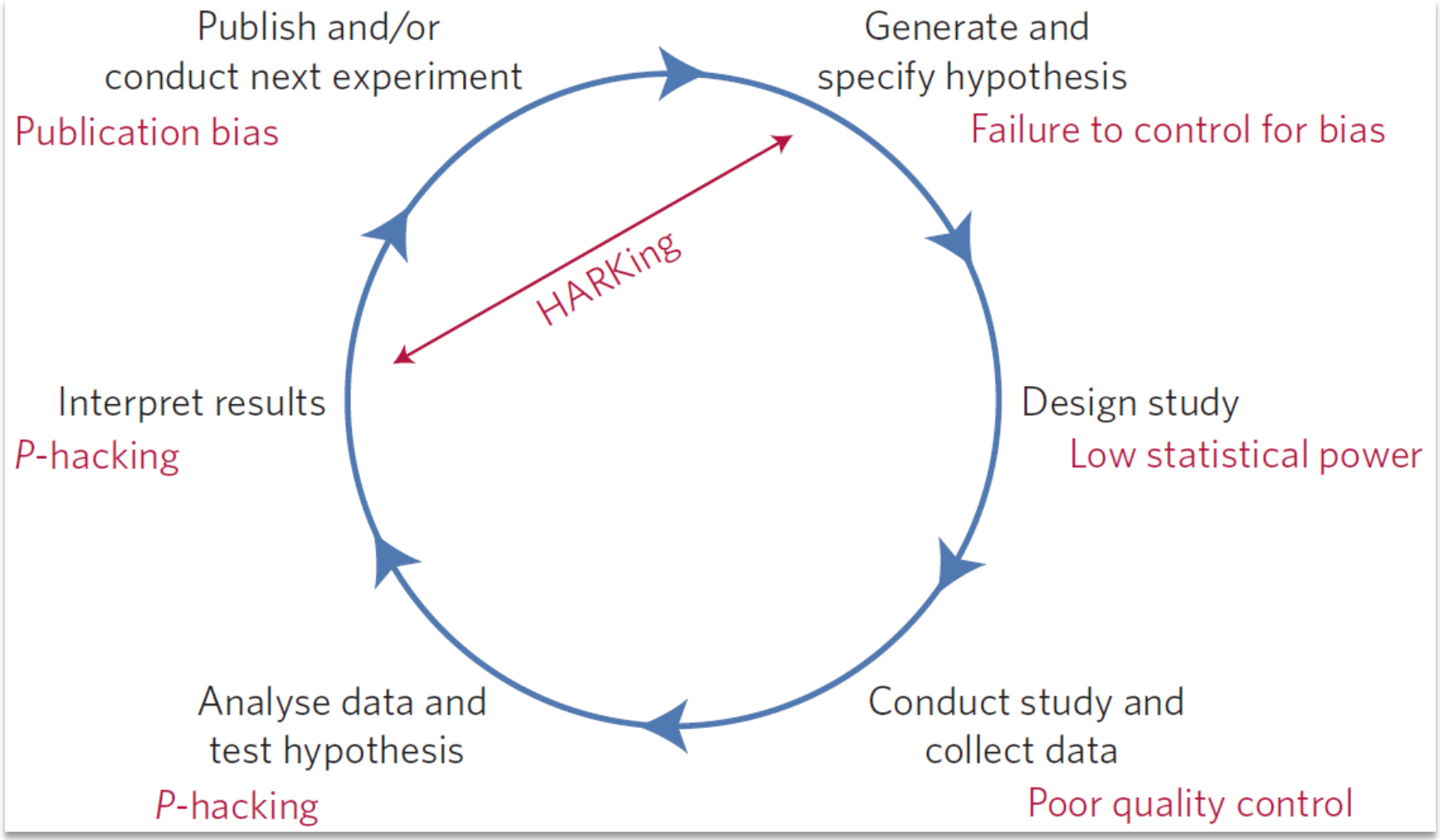
Communities of Rigor Champions to Change Culture

Table 1. Activities for communities of rigor champions to promote the principles of rigorous research.

Community	Intra-organizational activities	Inter-organizational activities
Trainees	• Promote transparency and other rigorous practices among colleagues and mentors • Advocate for resources to facilitate rigorous research practices	• Share institutional resources and practices in education and training • Call for changes in institutional culture and policies
Researchers	• Transparently report all experiments, including neutral outcomes • Promote rigorous practices among colleagues and trainees • Call for changes to institutional culture, policies, and infrastructure	• Share effective training practices and useful laboratory resources • Coordinate with the broader scientific community to promote better incentive structures
Educators	• Suggest improvements to available resources that address rigor • Integrate rigorous research principles into all coursework	• Share resources and educational best practices • Share effective learning evaluation methods
Institutional Leaders	• Enact policies and support infrastructure to incentivize transparency and other rigorous research practices • Explicitly incorporate mentoring, collaboration, and rigorous research practices into promotion procedures • Initiate and share outcomes from piloted educational resources	• Support and promote communities of rigor champions • Disseminate policy changes, new initiatives, educational successes, and implementation strategies • Develop tangible outcome measures to evaluate impact
Journal Editors and Reviewers	• Promote thorough review of research practices in publications • Explicitly support research transparency and neutral outcomes • Educate reviewers on which scientific practices are valued by the journal	• Collaborate to implement best practices consistently across different publishers
Scientific Societies and Organizations	• Support the founding of communities of rigor champions • Compile and encourage best practices used by the scientific community • Host workshops and educational materials for members	• Promote and maintain communities of rigor champions • Encourage institutional policies that promote research quality and effective education
Funding Organizations	• Emphasize attention to rigor in peer review • Reward rigorous research practices and outstanding mentorship • Support infrastructure for transparent and rigorous science • Support educational resources and initiatives	• Support and promote communities of rigor champions • Share best practices for incentivizing rigorous research and educating scientists • Develop partnerships to support better training and facilitate cultural changes

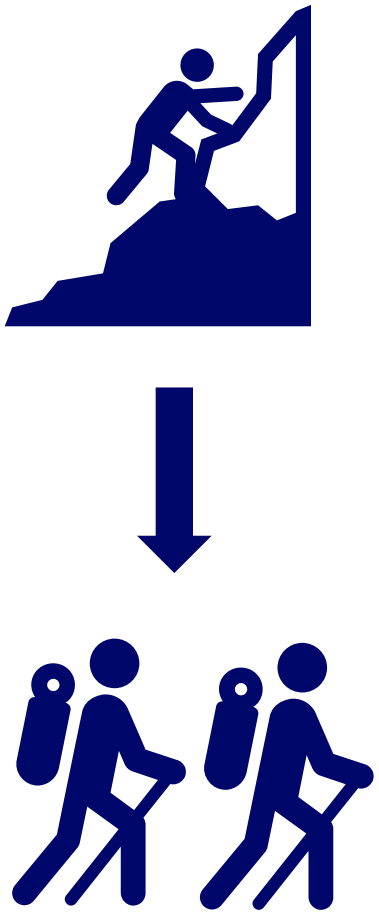
Koroshetz *et al.*, *eLife* 2020; 9: e55915

Feedforward Cycle of Low Research Quality



Modified from Munafò *et al.*, *Nature Human Beh* 2017; 1: 0021

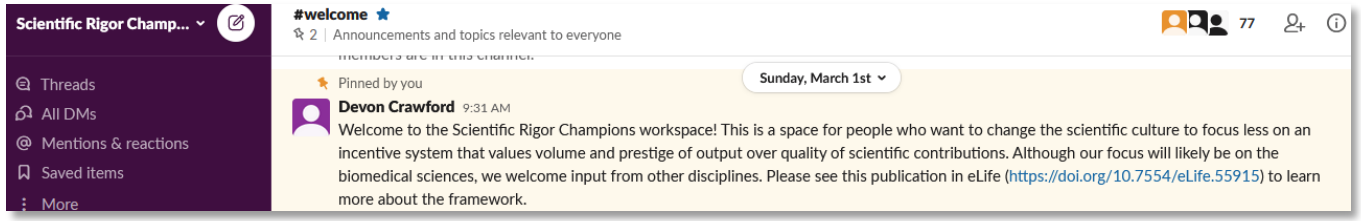
Small Changes Can Shift the Overall Enterprise



Modified from Malcolm Macleod, University of Edinburgh

NINDS Resources

- **NINDS Office of Research Quality:**
  - Website: *https://www.ninds.nih.gov/Current-Research/Trans-Agency-Activities/RigorAndReproducibility*
  - Email: *RigorChampions@nih.gov*
  - Slack Workspace: *ScientificRigor.slack.com*



- **NINDS List of Rigor Resources:**
  - *https://www.ninds.nih.gov/Current-Research/Trans-Agency-Activities/Rigor-Transparency/RigorChampionsAndResources*

Resources Table

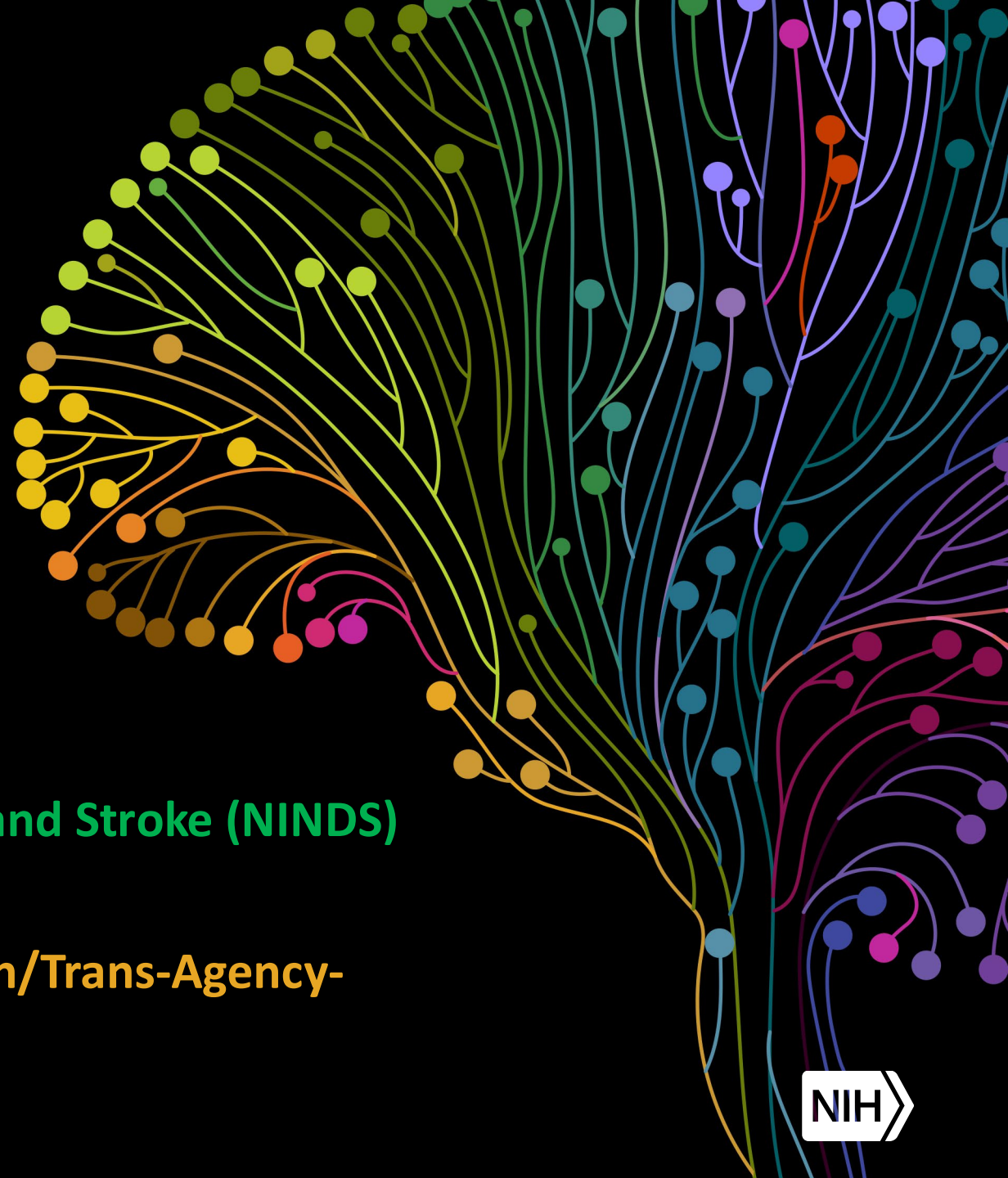
Categories of resources listed in the table include Books and Articles, Guidelines and Protocols, Organizations and Training Programs, Software and Other Digital Resources, and Videos and Courses.

Please use the drop-down menu under "Categories" to filter results based on one of these categories or use the "Quick Search" bar on the right to enter a key word of your choice.

Show 10 entries Quick Search:

Resource	Description	Category - All -
10 Simple Rules for Evaluating Model Credibility	Communication tool by IMAG (Interagency Modeling and Analysis Group) for modelers to organize their model development process	Guidelines and Protocols
2 Min Stats	Short, animated videos about statistics	Videos and Courses
A Call for Transparent Reporting to Optimize the Predictive Value of Preclinical Research	Article in Nature listing important experimental design elements to report in preclinical research papers	Books and Articles, Guidelines and Protocols

Thank You!



Devon Crawford, Ph.D.

Office of Research Quality

National Institute of Neurological Disorders and Stroke (NINDS)

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https://www.ninds.nih.gov/Current-Research/Trans-Agency-Activities/RigorAndReproducibility