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

Disorders  Funding  Current Research  News & Events  About NINDS

COVID-19

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Get the latest public health information from HHSC
Get the latest public health information from CDC

Home » Current Research » Trans-Agency Activities

NINDS Office of Research Quality

Experimental and analytical rigor, measures to reduce bias, and transparency of reporting are the foundations for quality scientific research. Attention to principles of good study design and transparent reporting are essential to enable the scientific community as well as the community at large to assess the value of scientific findings. This is also important for peer reviewers to properly advise NINDS on grant applications. Please visit the resources referenced below or contact us for more information.

Rigor Champions and Resources

NINDS held a workshop in October 2018 on how better to instill the principles of rigorous research, which brought together subject matter experts capable of evaluating current

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Related Announcements

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]
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!)
“[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 \textit{unintentional} and \textit{unconscious}. It is defined broadly as the \textit{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 \textit{making everything equal during the design, conduct and interpretation of a study, and reporting those steps in an explicit and transparent way.”}
“Randomised 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
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

Results from blind rater of Psychological Science

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

- Professional Standards
- Journals
- Institutions
- Funders
Scientists Experience Competing Pressures

- Professional Standards
- Journals
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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.
Spinal Cord Injury (SCI)

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
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).
### Table 1
Summary of FORE5G replication studies.

<table>
<thead>
<tr>
<th>Original article</th>
<th>Original finding</th>
<th>Result of replication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lu et al., 2002</td>
<td>Delayed transplant of olfactory glomeruli (OLF) improved hindlimb motor function after complete transection in rats.</td>
<td>No replication. No significant improvement in hindlimb function in rats that received OLF transplants.</td>
</tr>
<tr>
<td>Li and Stittmatter, 2003</td>
<td>Intraspinal delivery of NEP1-40 improves hindlimb motor function and enhances CST sprouting after thoracic dorsal hemisection in mice.</td>
<td>Partial replication. Enhancement of locomotor function in one of two replicate studies; no difference in CST axon growth.</td>
</tr>
<tr>
<td>Pearse et al., 2004</td>
<td>Combined treatment with Schwann cell transplants, Retinpar and intraspinal injection of bFGF Improves locomotor recovery after thoracic contusion in rats.</td>
<td>Mixed results. Rats that received Schwann cells only improved, but the combination treatment was not significantly better than single treatments.</td>
</tr>
<tr>
<td>Eckhardt et al., 2007</td>
<td>Intraspinal delivery of an EGF receptor antagonist (PD18833) enhances recovery of hindlimb motor and bladder function after thoracic contusion in rats.</td>
<td>No replication. Treatment group was significantly more impaired and lesion size was larger.</td>
</tr>
<tr>
<td>Bradbury et al., 2002</td>
<td>Intraspinal delivery of ChAT elevates regeneration of CST axons following cervical dorsal spinal cord injuries in rats.</td>
<td>Inconclusive because lesions spared CST in some rats. Not repeated because of other studies supporting original study.</td>
</tr>
<tr>
<td>Gotlo et al., 2002</td>
<td>Delivery of recombinant Human Erythropoietin (EPO) reduced injury severity and improved locomotor recovery after thoracic contusion and compression in rats.</td>
<td>No replication. No significant effect of treatment.</td>
</tr>
<tr>
<td>Lee et al., 2004</td>
<td>Mesonine treatment reduces cell death and improves hindlimb motor function after contusion injury.</td>
<td>No replication. No significant effect of treatment.</td>
</tr>
<tr>
<td>Gris et al., 2004</td>
<td>Treatment with a monoclonal antibody to the CD11d integrin subunit reduced infiltration of neutrophils, improved neurological outcomes, reduced neuropathic pain and morphological damage following spinal cord injury in rats.</td>
<td>Partial replication. There was a trend for greater recovery and reduced tissue damage, but differences were not statistically significant.</td>
</tr>
<tr>
<td>Wang et al., 2004</td>
<td>Intraspinal delivery of FGF7 receptor blockers or systemic administration of the FGF7 receptor antagonist Brilliant Blue G improved hindlimb locomotor function and reduced injury severity after thoracic contusion in rats.</td>
<td>No replication. Treatment groups did not differ significantly from controls.</td>
</tr>
<tr>
<td>Subral et al., 2007</td>
<td>Delivery of glibenclamide, which targets (SUR1)-regulated cation channels, attenuates secondary intraspinal hemorrhage and neuropathic pain following cervical spinal cord injury in rats.</td>
<td>Successfully replicated after discovering that the effect depended on the exact mechanism of injury.</td>
</tr>
<tr>
<td>Guth et al., 1994</td>
<td>Acute treatment with a combination of progesterone, UPS and indomethacin enhanced hindlimb locomotor function and reduced lesion size after thoracic spinal cord injury in rats.</td>
<td>Replicated but with less robust effects. Differences in outcomes assessment, drug composition and injury model may have degraded robustness of effect.</td>
</tr>
</tbody>
</table>

**NINDS Preclinical Spinal Cord Injury Replication Studies**

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)

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:**

- Kriz *et al.*, *Neurobiol Dis* 2002; 10: 268
- Van Den Bosch *et al.*, *NeuroReport* 2002; 13: 1067
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

DUE DILIGENCE, OVERDUE
Results of rigorous animal tests by the Amyotrophic Lateral Sclerosis Therapy Development Institute (ALS TDI) are less promising than those published. All these compounds have disappointed in human testing.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Published (%)</th>
<th>ALS TDI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riluzole*</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Creatine</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Celebrex</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Lithium</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Minocycline</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Sodium phenylbutyrate</td>
<td>20</td>
<td>15</td>
</tr>
<tr>
<td>Dexpramipexole</td>
<td>15</td>
<td>10</td>
</tr>
</tbody>
</table>

*Although riluzole is the only drug currently approved by the US Food and Drug Administration for ALS, our work showed no survival benefit.
†References for published studies can be found in supplementary information at go.nature.com/hk4q6c.
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.

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?

NINDS Workshop and “Landis 4” Paper

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

Landis et al., Nature 2012; 490: 187
NINDS Presentation to the NIH ACD

Advisory Committee to the Director (ACD) June 2013 - Day 1

Improving the quality of preclinical research through more rigorous study design and transparent reporting

Story Landis, PhD
Advisory Committee to the Director (ACD)
National Institutes of Health (NIH)
June 13-14, 2013


Story Landis
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. 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. Even if this represents only a fraction of the actual problem, such papers are vastly

• Training
• Grant applications
• Raw data
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.”

*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:

1. **Premise**: The scientific premise forming the basis of the proposed research
2. **Design**: Rigorous experimental design for robust and unbiased results
3. **Variables**: Consideration of relevant biological variables
4. **Authentication**: Authentication of key biological and/or chemical resources

“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.
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**

<table>
<thead>
<tr>
<th>Form</th>
<th>Section</th>
<th>Heading</th>
<th>Current language</th>
<th>Revised language</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Plan</td>
<td>Research Strategy Significance</td>
<td>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.</td>
<td>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.</td>
<td></td>
</tr>
<tr>
<td>Research Plan</td>
<td>Research Strategy Approach</td>
<td>Not Applicable</td>
<td></td>
<td>Describe plans to address weaknesses in the rigor of the prior research that serves as the key support for the proposed project.</td>
</tr>
</tbody>
</table>

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*.

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.

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.

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.

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?

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

NIH Resources for Publications and Grant Applications

Rigor and Reproducibility

Principles and Guidelines for Reporting Preclinical Research

NIH held a joint workshop in June 2014 with the Nature Publishing Group and Science on the issue of reproducibility and rigor of research findings, with journal editors representing over 30 basic/preclinical science journals in which NIH-funded investigators have most often published. The workshop focused on identifying the common opportunities in the scientific publishing arena to enhance rigor and further support research that is reproducible, robust, and transparent.

The journal editors came to consensus on a set of principles to facilitate these goals, which a considerable number of journals have agreed to endorse. These principles are shown below.

- Rigorous statistical analysis
- Transparency in reporting
- Data and material sharing
- Consideration of refutations
- Consider establishing best practice guidelines for:
  - Endorsements — Principles and Guidelines for Reporting Preclinical Research
  - Adapted Guidelines

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

Advisory Committee to the Director - June 2021 (Day 2)

Charge

- Identify gaps and opportunities to improve the rigor, reproducibility, translational validity, and transparency of animal models studies
- Evaluate how animal models of human disease are currently developed, validated, and accepted into routine use, and how this process could be improved
- Consider the process for validating alternative models to animal research
- Consider benefits and burdens of registering animal studies that aim to lead to first human trials
- Model financial implications of potential changes in the average costs of grants using animal models, the number of studies funded, or the need to develop consortia to achieve appropriate statistical power
- Consider how rigor in animal research is incorporated into training

Recommendations: Five Themes

1. Improve Study Design and Analytic Rigor
2. Address Bias, Incomplete Reporting, and Questionable Research Practices
3. Improve Relevance and Use of Animal Models
4. Improve Methodologic and Results Reporting
5. Measure and Evaluate Effectiveness and Costs

https://videocast.nih.gov/watch=42270
“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.”
Data Science Resources at NIH

https://datascience.nih.gov/
Scientists Experience Competing Pressures

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- Journals
- Institutions
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Scientists Experience Competing Pressures

- Professional Standards
- Journals
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Journal Checklists for Increasing Reporting Transparency

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 methods used was performed, describe how sample sizes were chosen and provided.

Data exclusions
Describe any data exclusions. If no data were excluded from the analysis, state the rationale behind them, indicating whether exclusion criteria were predefined.

Replication
Describe the measures taken to verify the reproducibility of the experiments. OR if there are any findings that were not replicated or cannot be replicated.

Randomization
Describe how samples/organisms/participants were allocated into experimental conditions. If randomization was controlled or if this is not relevant to your study, explain why.

Blinding
Describe whether the investigators were blinded to group allocation. If yes, describe how. 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 & References 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 strategies for biologists contains articles on many of the points above.

https://www.nature.com/documents/nr-reporting-summary.pdf
Journal Checklists Improve Reporting

Control journals

Sample size calculation:

Randomization:

Blinding:

Data exclusions:

NPG journals

Scientists Experience Competing Pressures

- Professional Standards
- Journals
- Institutions
- Funders
Scientific Transparency at Conferences

Shake up conferences

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

Silberberg et al., Nature 2017; 548: 153
Scientists Experience Competing Pressures

- Professional Standards
- Journals
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- Funders
Efforts to Change Hiring and Promotion/Tenure Practices

“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

- **Professional Standards**
- **Journals**
- **Institutions**
- **Funders**
<table>
<thead>
<tr>
<th>Community</th>
<th>Intra-organizational activities</th>
<th>Inter-organizational activities</th>
</tr>
</thead>
</table>
| 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

Research Improvement Strategy

Experiments (N)

Research Quality

CAMARADES: Bringing evidence to translational medicine

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](https://www.ninds.nih.gov/Current-Research/Trans-Agency-Activities/RigorAndReproducibility)
  - Email: [RigorChampions@nih.gov](mailto:RigorChampions@nih.gov)
  - Slack Workspace: [ScientificRigor.slack.com](https://ScientificRigor.slack.com)

- **NINDS List of Rigor Resources:**
  - [https://www.ninds.nih.gov/Current-Research/Trans-Agency-Activities/Rigor-Transparency/RigorChampionsAndResources](https://www.ninds.nih.gov/Current-Research/Trans-Agency-Activities/Rigor-Transparency/RigorChampionsAndResources)
Thank You!

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