



Reproducibility in biomedical research  
12.04.2024

# Transparency in statistical reporting in preclinical science

Romain-Daniel Gosselin, PhD

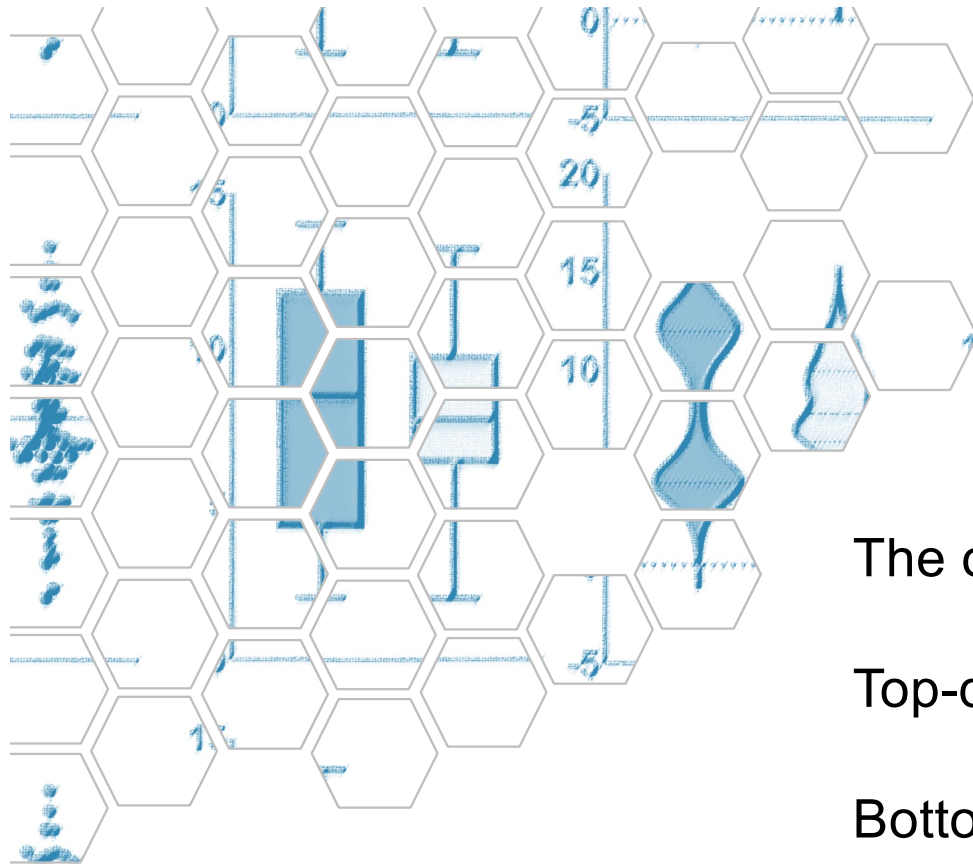
*Precision medicine unit*

*Centre Hospitalier Universitaire Vaudois*

*Lausanne*



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et de médecine



The outline of the problem

Top-down avenues: guidelines and requirements

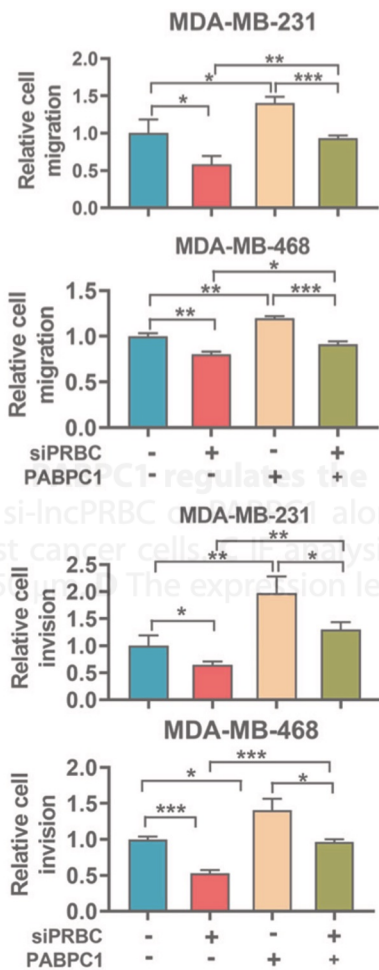
Bottom-up strategies: education

## **Statistics analysis**

Statistical analysis was performed using GraphPad Prism 8.0 software (La Jolla, CA, USA). Data are presented as mean  $\pm$  standard deviation (SD) from at least three independent experiments. Student's *t* test were used to compare the difference between two groups. One-way ANOVA analysis was performed for more than three groups. Kaplan-Meier method and log-rank analysis were used for survival analysis.  $P < 0.05$  was considered statistically significant.

## **DATA AVAILABILITY**

The data in this study are available from the corresponding author upon reasonable request.



**Fig. 6** *IncRNA PRBC* regulates the biological function of *IncRNA PRBC* in breast cancer. MDA-MB-231 and MDA-MB-468 cells were transfected with si-*IncPRBC* alone or in combination. Transwell assay was performed to explore the migratory (A) and invasive (B) abilities of breast cancer cells. Statistical analysis was conducted to determine the LC3 expression in breast cancer cells treated with 10 nM rapamycin. Scale bar, 50 μm. The expression levels of autophagy-related proteins were investigated using western blotting. (\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ ).

### Statistics analysis

Statistical analysis was performed using GraphPad Prism 8.0 software (La Jolla, CA, USA). Data are presented as mean  $\pm$  standard deviation (SD) from at least three independent experiments. Student's *t* test were used to compare the difference between two groups. One-way ANOVA analysis was performed for more than three groups. Kaplan-Meier method and log-rank analysis were used for survival analysis.  $P < 0.05$  was considered statistically significant.

### DATA AVAILABILITY

The data in this study are available from the corresponding author upon reasonable request.

Sample size? (Experimental units, sampling units)

Exact values / raw data?

Blinding? Randomization?

Software (and version)?

Student's t-test laterality?

Method (post-test) for multiple testing?

Exact p-values?...

Ethical issue



Waste of resources

Epistemological crisis



Guidelines	Requirements	Education
<p>Recommend the adoption of correct statistical practices</p>	<p>Pragmatically enforce easy-to-change new practices</p>	<p>Ensure enough understanding of basic statistical concepts</p>
<p>Often field specific Proven limited impact</p>	<p>Often field specific Higher impact</p>	<p>Possible transdisciplinarity</p>

### Guidelines

Recommend the adoption of correct statistical practices

Often field specific  
Proven limited impact

### Requirements

Pragmatically enforce easy-to-change new practices

Often field specific  
Higher impact

### Education

Ensure enough understanding of basic statistical concepts

Possible transdisciplinarity



## Reporting ethical matters in *The Journal of Physiology*: standards and advice

Gordon B. Drummond

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Reporting of ethical matters in *The Journal* is very important. To advise and assist authors, particularly those who may be less familiar with the legislation in the UK, this article sets out the basic principles and methods that should be used and provides many key web sources of information. It addresses the structure of regulations, and introduces the concept of research governance. The UK law is summarized. Advice is given on the format and description of experiments, and common problems addressed. Aspects of human studies are addressed. Ethical considerations of publication such as authorship and originality, and problems such as plagiarism and fabrication are described. Updates will be published regularly.

*The Journal of Physiology* has two specific features that require substantial details of the ethical aspects of studies. First, *The Journal* aims to meet the highest ethical standards. Since it is read by those with a general as well as a specific interest, reports need to be intelligible to the general reader. Second there are no strict restrictions to contribution size. For these reasons in particular, *The Journal* expects full and careful reporting of the ethical details of studies. The standards applied by *The Journal* are based on UK legislation. Nevertheless, the composition of the Editorial Board and the readership of *The Journal* are world-wide, and the policies that deal with ethical matters have to encompass this. This article explains and expands the guidance for authors, and indicates where problems frequently occur, but is not intended to replace the guidance. If necessary, reference to this article may assist authors to prepare a manuscript for submission.

### Animal studies

Setting ethical standards in scientific research is not simple, and the use of animals in research is a contentious issue. The sources of our ethical beliefs are varied. Different views allow different degrees of 'moral importance' to be drawn by different individuals; indeed some views in society may be diametrically opposed. Chapters 11 and 12 of the independently commissioned publication *The Use of Non-human Primates in Research* give a useful summary and overview of these problems, although in a single specific context.

<http://www.acmedsci.ac.uk/p99puid83.html>

Although opinions differ, there are central principles of ethical conduct that are clear and should always be followed. Simply and practically stated, each study should be reported in a way that allows the general reader to appreciate that it has been carried out properly, without causing unnecessary pain and suffering to animals. (In the case of human studies, the reader should be told that proper consent was obtained.) In addition the reader must appreciate exactly which regulations were applied to the study, and that those regulations were properly supervised.

Similar ethical standards are regulated by law in many countries. Making sure that suitable ethical standards are not only regulated but are also met and followed is important in the publication of research findings. *The Journal of Physiology* has standards derived from UK legislation on animal work which are among the most exacting in the world. Clearly, scientific work done in other countries has to comply with the laws of that particular country. *The Journal* will need to know that the standards and regulations used are equivalent to those of the UK if the work is to be published in *The Journal of Physiology*. In fact, although the UK laws regulate much of the fine detail of conduct, the regulations are careful not to define the exact structure of regulation to be used. The law establishes the principles, and requires each scientific establishment to make suitable local provisions. The present article lists and explains the standards and processes that must be followed by work described in *Journal of Physiology* articles. The principal points covered are those summarized by our guidance to authors provided by *The*

**Experimental procedures.** The fundamental criterion is to give a description that would allow the study to be replicated by a similarly trained research worker.





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PERSPECTIVE

# The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research

Nathalie Percie du Sert <sup>1\*</sup>, Viki Hurst<sup>1</sup>, Amrita Ahluwalia <sup>2,3</sup>, Sabina Alam <sup>4</sup>, Marc T. Avey <sup>5</sup>, Monya Baker<sup>6</sup>, William J. Browne <sup>7</sup>, Alejandra Clark <sup>8</sup>, Innes C. Cuthill <sup>9</sup>, Ulrich Dirnagl <sup>10</sup>, Michael Emerson<sup>11</sup>, Paul Garner <sup>12</sup>, Stephen T. Holgate<sup>13</sup>, David W. Howells <sup>14</sup>, Natasha A. Karp <sup>15</sup>, Stanley E. Lazic<sup>16</sup>, Katie Lidster<sup>1</sup>, Catriona J. MacCallum <sup>17</sup>, Malcolm Macleod <sup>18</sup>, Esther J. Pearl <sup>1</sup>, Ole H. Petersen <sup>19</sup>, Frances Rawle <sup>20</sup>, Penny Reynolds <sup>21</sup>, Kieron Rooney <sup>22</sup>, Emily S. Sena <sup>18</sup>, Shai D. Silberberg<sup>23</sup>, Thomas Steckler <sup>24</sup>, Hanno Würbel <sup>25</sup>

**PLOS BIOLOGY**

<https://doi.org/10.1371/journal.pbio.3000410>

- ARRIVE guidelines >
- Essential 10 ^
- 1. Study Design >
- 2. Sample size >
- 3. Inclusion and exclusion criteria >
- 4. Randomisation >
- 5. Blinding/Masking >
- 6. Outcome measures >
- 7. Statistical methods >
- 8. Experimental animals >
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- 10. Results >
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## The ARRIVE guidelines 2.0

This section of the website provides detailed explanations about each item of the guidelines. Use the left-hand side menu to navigate to each item. The guidelines in their entirety can also be downloaded as a PDF, in [English](#) or a variety of [translations](#).

To facilitate a step-wise approach to improving reporting, the guidelines are organised into two prioritised sets:

### ARRIVE Essential 10

These ten items are the basic minimum that must be included in any manuscript describing animal research. Without this information readers and reviewers cannot assess the reliability of the findings.

### Recommended Set

These items complement the Essential 10 set and add important context to the study described. Reporting the items in both sets represents best practice.

Each item of the guidelines includes examples of good reporting from the published literature, extracted from different types of studies, in model organisms ranging from mammals to invertebrates. This battery of examples will be regularly expanded.

Consulting this information during the planning of an animal study ensures that researchers can benefit from the explanations and advice on experimental design, minimisation of bias, sample size and statistical analyses, helping the design of rigorous and reliable *in vivo* experiments.

The Explanation and Elaboration for the ARRIVE guidelines 2.0 were originally published in *PLOS Biology* [doi:10.1371/journal.pbio.3000411](https://doi.org/10.1371/journal.pbio.3000411) under a CC-BY license.

## The ARRIVE Essential 10

These items are the basic minimum to include in a manuscript. Without this information, readers and reviewers cannot assess the reliability of the findings.

<b>Study design</b>	1	For each experiment, provide brief details of study design including: <ol style="list-style-type: none"> <li>The groups being compared, including control groups. If no control group has been used, the rationale should be stated.</li> <li>The experimental unit (e.g. a single animal, litter, or cage of animals).</li> </ol>
<b>Sample size</b>	2	<ol style="list-style-type: none"> <li>Specify the exact number of experimental units allocated to each group, and the total number in each experiment. Also indicate the total number of animals used.</li> <li>Explain how the sample size was decided. Provide details of any <i>a priori</i> sample size calculation, if done.</li> </ol>
<b>Inclusion and exclusion criteria</b>	3	<ol style="list-style-type: none"> <li>Describe any criteria used for including and excluding animals (or experimental units) during the experiment, and data points during the analysis. Specify if these criteria were established <i>a priori</i>. If no criteria were set, state this explicitly.</li> <li>For each experimental group, report any animals, experimental units or data points not included in the analysis and explain why. If there were no exclusions, state so.</li> <li>For each analysis, report the exact value of <i>n</i> in each experimental group.</li> </ol>
<b>Randomisation</b>	4	<ol style="list-style-type: none"> <li>State whether randomisation was used to allocate experimental units to control and treatment groups. If done, provide the method used to generate the randomisation sequence.</li> <li>Describe the strategy used to minimise potential confounders such as the order of treatments and measurements, or animal/cage location. If confounders were not controlled, state this explicitly.</li> </ol>
<b>Blinding</b>	5	Describe who was aware of the group allocation at the different stages of the experiment (during the allocation, the conduct of the experiment, the outcome assessment, and the data analysis).
<b>Outcome measures</b>	6	<ol style="list-style-type: none"> <li>Clearly define all outcome measures assessed (e.g. cell death, molecular markers, or behavioural changes).</li> <li>For hypothesis-testing studies, specify the primary outcome measure, i.e. the outcome measure that was used to determine the sample size.</li> </ol>
<b>Statistical methods</b>	7	<ol style="list-style-type: none"> <li>Provide details of the statistical methods used for each analysis, including software used.</li> <li>Describe any methods used to assess whether the data met the assumptions of the statistical approach, and what was done if the assumptions were not met.</li> </ol>
<b>Experimental animals</b>	8	<ol style="list-style-type: none"> <li>Provide species-appropriate details of the animals used, including species, strain and substrain, sex, age or developmental stage, and, if relevant, weight.</li> <li>Provide further relevant information on the provenance of animals, health/immune status, genetic modification status, genotype, and any previous procedures.</li> </ol>
<b>Experimental procedures</b>	9	For each experimental group, including controls, describe the procedures in enough detail to allow others to replicate them, including: <ol style="list-style-type: none"> <li>What was done, how it was done and what was used.</li> <li>When and how often.</li> <li>Where (including detail of any acclimatisation periods).</li> <li>Why (provide rationale for procedures).</li> </ol>
<b>Results</b>	10	For each experiment conducted, including independent replications, report: <ol style="list-style-type: none"> <li>Summary/descriptive statistics for each experimental group, with a measure of variability where applicable (e.g. mean and SD, or median and range).</li> <li>If applicable, the effect size with a confidence interval.</li> </ol>

## The Recommended Set

These items complement the Essential 10 and add important context to the study. Reporting the items in both sets represents best practice.

<b>Abstract</b>	11	Provide an accurate summary of the research objectives, animal species, strain and sex, key methods, principal findings, and study conclusions.
<b>Background</b>	12	<ol style="list-style-type: none"> <li>Include sufficient scientific background to understand the rationale and context for the study, and explain the experimental approach.</li> <li>Explain how the animal species and model used address the scientific objectives and, where appropriate, the relevance to human biology.</li> </ol>
<b>Objectives</b>	13	Clearly describe the research question, research objectives and, where appropriate, specific hypotheses being tested.
<b>Ethical statement</b>	14	Provide the name of the ethical review committee or equivalent that has approved the use of animals in this study, and any relevant licence or protocol numbers (if applicable). If ethical approval was not sought or granted, provide a justification.
<b>Housing and husbandry</b>	15	Provide details of housing and husbandry conditions, including any environmental enrichment.
<b>Animal care and monitoring</b>	16	<ol style="list-style-type: none"> <li>Describe any interventions or steps taken in the experimental protocols to reduce pain, suffering and distress.</li> <li>Report any expected or unexpected adverse events.</li> <li>Describe the humane endpoints established for the study, the signs that were monitored and the frequency of monitoring. If the study did not have humane endpoints, state this.</li> </ol>
<b>Interpretation/scientific implications</b>	17	<ol style="list-style-type: none"> <li>Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature.</li> <li>Comment on the study limitations including potential sources of bias, limitations of the animal model, and imprecision associated with the results.</li> </ol>
<b>Generalisability/translation</b>	18	Comment on whether, and how, the findings of this study are likely to generalise to other species or experimental conditions, including any relevance to human biology (where appropriate).
<b>Protocol registration</b>	19	Provide a statement indicating whether a protocol (including the research question, key design features, and analysis plan) was prepared before the study, and if and where this protocol was registered.
<b>Data access</b>	20	Provide a statement describing if and where study data are available.
<b>Declaration of interests</b>	21	<ol style="list-style-type: none"> <li>Declare any potential conflicts of interest, including financial and non-financial. If none exist, this should be stated.</li> <li>List all funding sources (including grant identifier) and the role of the funder(s) in the design, analysis and reporting of the study.</li> </ol>

The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. Originally published in *PLOS Biology*, July 2020.





Guidelines for reporting statistics in journals published by the American Physiological Society <https://doi.org/10.1152/ajpendo.00213.2004>

Guidelines for reporting statistics in journals published by the American Physiological Society: the sequel <https://doi.org/10.1152/advan.00022.2007>

Douglas Curran-Everett<sup>1,2,3</sup> and Dale J. Benos<sup>4</sup>

<sup>1</sup>Division of Biostatistics, National Jewish Medical and Research Center, and Departments of <sup>2</sup>Preventive Medicine and Biometrics and <sup>3</sup>Physiology and Biophysics, School of Medicine, University of Colorado at Denver and Health Sciences Center, Denver, Colorado; and <sup>4</sup>Department of Physiology and Biophysics, University of Alabama, Birmingham, Alabama

Table 1. American Physiological Society journal manuscripts in 1996, 2003, and 2006: reporting of statistics

	n			Standard Deviation			Standard Error			Confidence Interval			Precise P Value		
	1996	2003	2006	1996	2003	2006	1996	2003	2006	1996	2003	2006	1996	2003	2006
<i>Am J Physiol</i>															
<i>Cell Physiol</i>	43	30	322	21	20	19	88	73	78	0	0	1	7	13	13
<i>Endocrinol Metab</i>	28	28	302	18	7	13	86	89	87	0	4	2	4	39*	30
<i>Gastrointest Liver Physiol</i>	26	28	272	8	25	24	92	79	77	0	0	2	4	14	17
<i>Heart Circ Physiol</i>	60	62	627	17	23	22	87	76	77	0	5	1	10	19	20
<i>Lung Cell Mol Physiol</i>	25	26	261	20	19	22	84	88	81*	0	0	2	4	19	18
<i>Regul Integr Comp Physiol</i>	41	29	384	17	10	12	88	90	90	0	0	1	15	41*	27
<i>Renal Physiol</i>	27	25	289	15	12	15	93	80	79	0	4	1	7	4	17*
<i>J Appl Physiol</i>	62	57	519	24	39	35	79	67	65	0	7*	4	6	26*	34
<i>J Neurophysiol</i>	58	61	699	36	23	30	69	64	57	2	5	6	5	30*	38

# Insufficient transparency of statistical reporting in preclinical research: a scoping review

Romain-Daniel Gosselin

**scientific** reports

<https://doi.org/10.1038/s41598-021-83006-5>

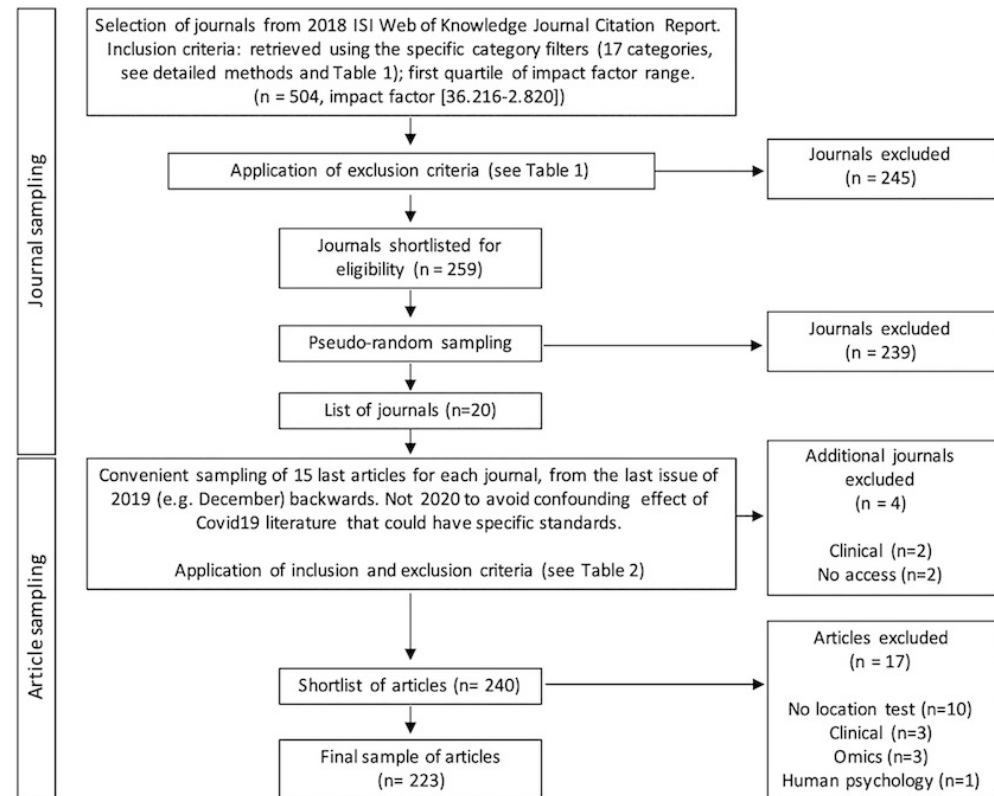
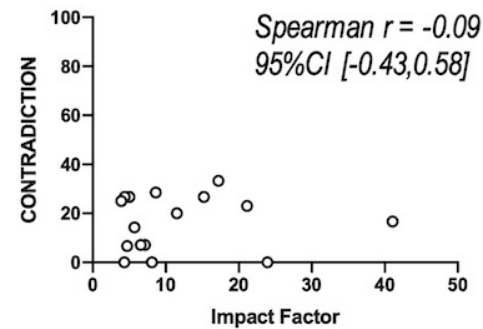
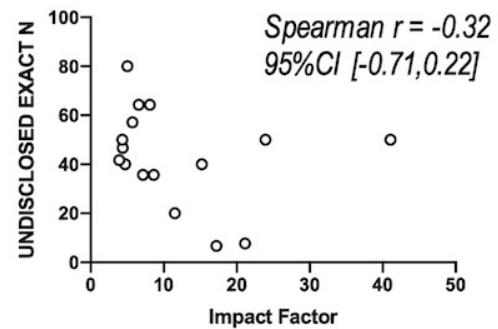
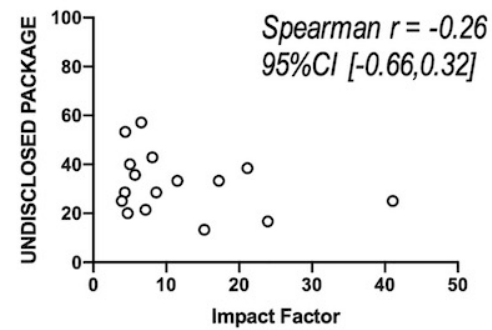
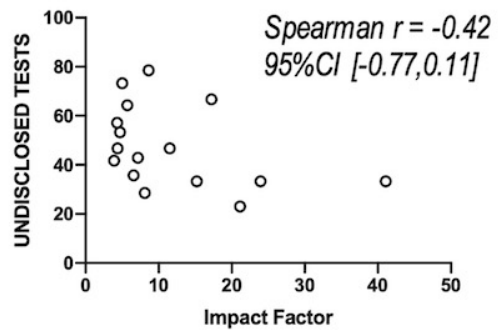
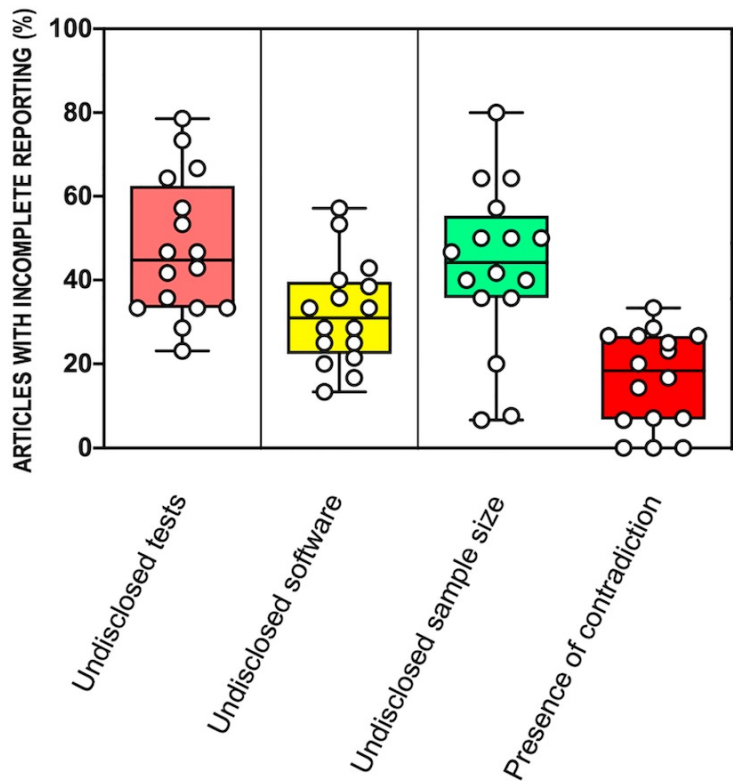


Figure 4. Flow chart of the sampling protocol.



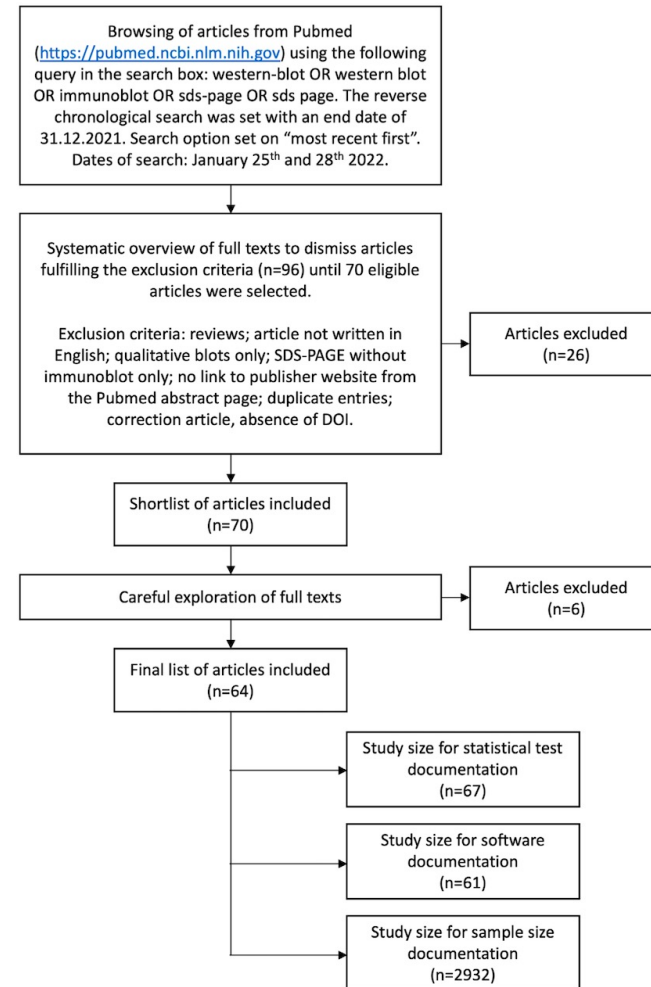


# A snapshot of statistical methods used in experimental immunoblotting: a scoping review

Romain-Daniel Gosselin\* 

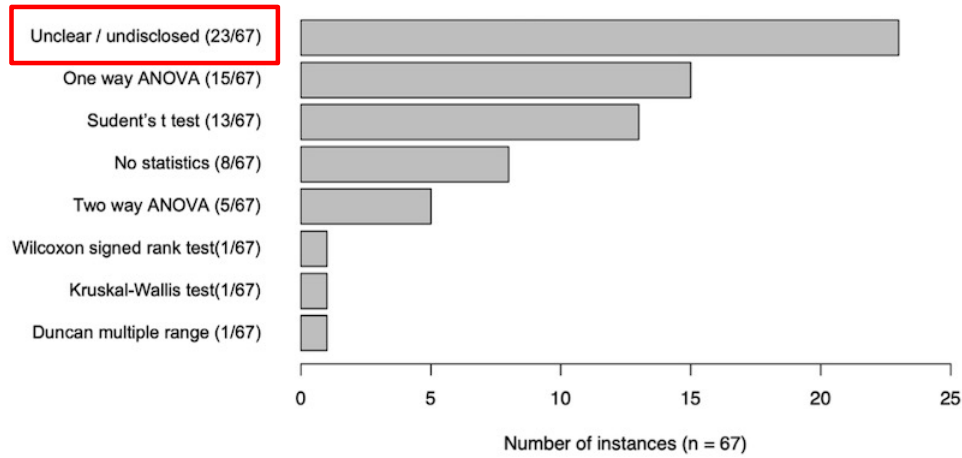


<https://doi.org/10.1051/fopen/2022009>



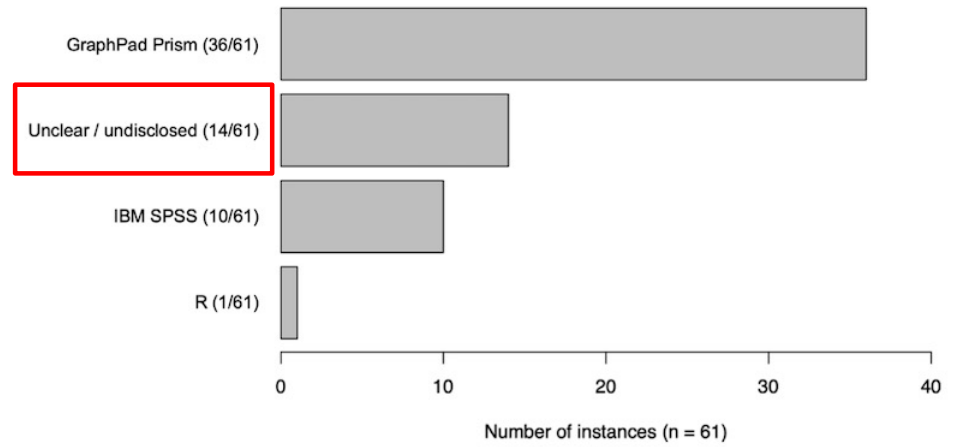
A

### Statistical tests



B

### Statistical software



### Guidelines

Recommend the adoption of correct statistical practices

Often field specific  
Proven limited impact

### Requirements

Pragmatically enforce easy-to-change new practices

Often field specific  
Higher impact

### Education

Ensure enough understanding of basic statistical concepts

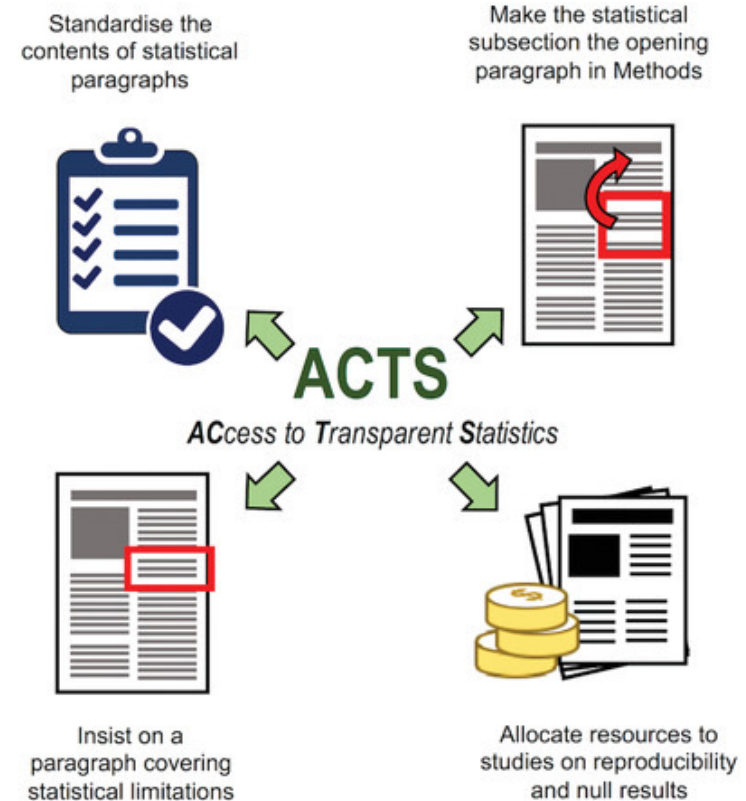
Possible transdisciplinarity

# Statistical Analysis Must Improve to Address the Reproducibility Crisis: The ACcess to Transparent Statistics (ACTS) Call to Action

Romain-Daniel Gosselin

BioEssays

<https://doi.org/10.1002/bies.201900189>



### Guidelines

Recommend the adoption of correct statistical practices

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Possible transdisciplinarity

## Elective courses: Doctoral programmes in Romandie

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563 PhD students since 2013

Lecture series over 2-3 days (usually 14-20 hours)

Introductory without (heavy) mathematics

Basics and bench utility (behaviour, cell biology, pharmacology...)

No programming

Focus on debunking misconceptions and misuse

Mostly *ex cathedra*

Reverse learning and problem-based learning

Workshops/case studies/reviewing occasionally

Polls, quizzes, discussions

*News*

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## **Call for submissions: Special issue on short introductory notes on biostatistics**

**Romain-Daniel Gosselin<sup>1</sup> and Penelope S Reynolds<sup>2</sup>**





# Call for submissions: Special issue on short introductory notes on biostatistics



More than 20 pre-submission abstracts received, 13 selected for submission

Additional 13 Invited contributors

Final inclusion of ~18-22 articles

Expected publication: Summer 2024



Thank you.

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