

Short Report



Animal researchers' views on the publication of negative results and subsequent policy adoptions

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Abstract

For over a decade, the non-publication of negative results from preclinical studies has been identified as a significant concern in biomedical research. Such underreporting is considered a contributor to the reproducibility crisis in the field and has been recognized by significant journals such as *Science* and *Nature*. In response to the consistently high non-publication rates of preclinical animal research in Europe, a survey was conducted among the biomedical research community to gather their views on publishing negative results. Using the EUSurvey platform, over 200 researchers directly working with animals were surveyed. The study aimed to understand the frequency of negative results, the reasons behind their non-publication, and the perceived pros and cons of making such results public. Insights from the survey could guide steps toward promoting transparency in science, refining research methodologies, reducing animal usage in experiments and minimizing research waste.

Keywords

3Rs, ethics and welfare, public policy, reduction

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Introduction

Scientists have identified the lack of publication of negative results of preclinical studies as a primary problem in biomedical research for over a decade. 1,2 The low dissemination of studies presenting negative findings has partially been blamed for the reproducibility crisis in biomedical research³ and has consequently been highlighted in editorials in prestigious journals such as Science⁴ and Nature⁵ as an important scientific issue to address. Publishing negative results is crucial for mitigating publication bias, which occurs when positive findings are disproportionately represented in literature. This bias skews the scientific record, making it difficult to form accurate conclusions and often leading to wasteful redundancy in research efforts. By including negative outcomes, the scientific community gains a more comprehensive understanding of research topics, facilitating progress by acknowledging what does not work. This approach fosters a culture of openness, improves resource allocation and upholds the integrity of scientific inquiry by presenting a balanced view of research findings.

In animal research, publishing negative results is especially important to avoid unnecessary repetition of experiments, ensuring the ethical use of animals. It contributes to the refinement and reduction of animal use by informing the scientific community about methodologies or hypotheses that have been disproven, thus guiding future research toward more promising directions. This practice enhances the welfare of animals used in research by maximizing the value of the data obtained from each experiment and adhering to the principles of responsible scientific conduct.

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However, negative studies are still seldom published in regular journals, and dedicated journals such as the *Journal of Negative Results in BioMedicine* are closing due to the low number of submissions. The clinical research community has recognized the challenge of finding suitable platforms for publishing negative results. An online tool, as mentioned by Bernard et al.,⁶ assists researchers in locating appropriate venues for such findings. However, only general-purpose repositories like Zenodo, Dryad or OSF.io often offer free avenues for submitting negative outcomes, underscoring the need for more dedicated spaces in scientific publishing landscapes.

Materials and methods

Wieschowski et al. highlight that approximately onethird of animal studies go unreported, with van der Naald et al.⁸ adding that around 74% of animals used in preclinical research are never mentioned in publications. This indicates a significant gap in the reporting of animal research findings. Given this situation, we asked the biomedical research community about their perceptions of publishing negative results. In particular, we were interested in determining how frequently researchers generate negative results, their opinions on the key causes for them, why they are typically not published, how they think they should be published, and the advantages and disadvantages of making them public. We used the EUSurvey platform to survey more than 200 researchers directly working with animals. (The survey transcript, its synopsis, study results and de-identified survey data are publicly available on the Open Science Framework, https://osf. io/9p7kz/)

The survey was distributed to all members listed in the 'Members' section on the website of the Federation of European Laboratory Animal Science Associations. In addition to this, we informed specific contacts about our survey: 12 in Sweden, 11 in Spain, seven in the UK, two each in Norway and the Netherlands and one each in Portugal, Ireland, Italy, Belgium and Germany. A total of 237 researchers completed the survey in its entirety (of a total of 241 respondents). The detailed profile of respondents is available on the Open Science Framework (OSF) link mentioned above. The most common profile of respondents was that of female academic researcher (59%), either established (32%) or in a leading position (29%), predominantly working in Spain or Germany (40%) and mainly dealing with mice (80%) or rats (46%).

Results

On average, respondents estimated that about onethird of their experiments finished with negative results, and that of these experiments, less than one-quarter could be published (generally along with other experiments yielding positive results). Both facts together imply that about one in four experiments are never reported. These numbers agree with those reported in Wieschowski et al. and van der Naald et al.^{7,8}

As a result, our survey shows that most biomedical researchers (about 95%) think that the animal research community should promote sharing research data and reports from negative experiments. From now on, we will put the percentage of respondents supporting a given statement in parentheses. Most questions were answered using a five-point Likert scale, but we typically condensed them into a three-point scale to ease the presentation of the results. Readers who are interested in the detailed results can refer to the OSF link provided above. A study summary is shown in Appendix 1 at the end of this article. The most common arguments for the promotion of sharing included:

- Avoiding repetitions of experiments (49%) that have already been carried out elsewhere but are unknown because their results have not been made public will reduce the money, time and animal lives spent on redundant research (32%).
- Negative results can be very helpful in designing new experiments, formulating new hypotheses about biological processes, and identifying variables that may affect the results of an experiment (39%). A previous negative result for a similar experiment may not prevent the execution of another experiment on the same topic. Instead, it could promote a better experimental design and more careful execution to avoid possible pitfalls of the previous attempt (11%).
- Researchers have an ethical obligation towards the animals participating in the experiments and the research community and society at large to share results (9%). Especially, there is a general agreement that all results (positive or negative) from public funding should be made public (95%).
- Finally, having a complete picture of the number of positive and negative results from similar experiments would significantly reduce the publication bias toward positive results (8%). This issue can significantly impact the validity of the results of systematic reviews with meta-analyses performed on published literature.

About 10% of the researchers raised concerns about the validity of having access to negative results. They Sorzano et al. 3

argued that a negative result could be due to a bad experimental design, important flaws in the execution of the experiment, or its statistical analysis. Some researchers questioned the usefulness of having such negative results available (less than 5%).

According to the surveyed researchers, the leading causes of negative results are a true lack of difference between groups or correlation between variables (80%), the variability of the observed variables (which may be underestimated before experimenting (80%)), a low sample size (67%), animal, environmental or other unknown factors (66%), execution, methodological or procedural mistakes (38%), the lack of control of other external variables (33%) and the gap between in vitro and in vivo experiments (27%).

The reasons argued for not publishing negative experiments included the general belief that papers reporting negative results are not accepted by journals (especially high-impact journals (93%)), that even if they are published, they do not get a large number of citations (72%) and that there are no institutional or community incentives to publish (67%). This is combined with pressure to publish positive results (publishing negative results would take precious time and energy from them without them being obliged to do so (58%)). Additionally, there is a lack of a culture of publishing negative results (94%), with researchers afraid of losing their scientific reputation and future grant opportunities (58%). Ultimately, there is always the honest doubt that a negative result reflects an absence of differences between groups or correlation between variables, or the absence of positive results is due to an experimental or design mistake hiding the true positive result underneath (49%). The presence of positive and negative controls in the experiment is critical to determine whether the experiment was well conducted. It is essential to recognize that the questions in this section were phrased as, 'What are the reasons you think other researchers do not publish their negative results?', which is a more indirect approach than directly asking, 'Why do you not publish negative results?'. This indirect method of questioning depersonalizes the query, which can frequently lead to more honest and accurate responses.

Based on career status, established (R3) and leading (R4) researchers chose not to publish negative results at a higher rate (56–59%) compared with student (R1) or early-career (R2) researchers (40–41%). This difference was statistically significant with an analysis of variance *p*-value of 0.035. However, no noticeable differences were observed between genders concerning this choice.

Researchers favour publishing negative results in a platform that is easily accessible for discovery (89%), offers citable content (80%), ensures quality control before publication (79%), is user-friendly for

navigation and submission (78%), allows free publishing (77%), supports full papers in peer-reviewed journals (70%), is affiliated with a reputable institution (66%), includes peer-review processes (58%) or provides a non-peer-reviewed, free-format repository (57%). They also value platforms that enable comments (57%) and are part of an open-science database (52%).

Researchers agree that funding agencies and scientific institutions should require that negative results be published (79%). They also agree that scientific societies should promote this practice (97%). However, there was no agreement on whether this decision to publish negative results or not should be left to the researcher (50%). There was also no agreement either on whether the laboratories or the individual researchers should be rewarded in some way for publishing negative results (less than 40% in all related questions).

When asked how they would prefer to share negative results, participants indicated that they preferred writing a full paper and submitting it to an open-access, peer-reviewed journal without any publishing cost (70%). For them, it would be important that this journal is hosted at some recognized institution (66%) and that it allows comments from other researchers (57%).

Discussion

From this survey, we conclude that: 1) scientists consider the sharing of negative results to be essential for science, society, the 3Rs, and an ethical aspect of research; 2) they are willing to do it with a standard as high as for positive results; 3) but they see severe drawbacks, mainly in the scientific culture, publishing options and lack of institutional or community incentives. Despite the encouragement by scientists and scientific journals of the publication of negative results, in practice, all these drawbacks result in a deficient proportion of negative results being published and a quarter of experiments never being reported.

The fact that established (R3) and leading (R4) researchers exhibit a greater tendency not to disclose results compared with their student (R1) or early-career (R2) counterparts may have several reasons: 1) a higher likelihood of encountering negative or inconclusive results throughout their careers, 2) the conduct of preliminary or pilot studies that may not yield definitive outcomes, 3) reduced publication pressure, given their established status, 4) a distinct approach to sharing findings, reflective of generational or disciplinary cultures. Additional considerations might also play a role, such as: 5) a greater involvement in confidential or proprietary research, limiting the scope for public disclosure, 6) a more strategic approach to publication, choosing to report only the most impactful findings,

7) the potential for more complex, long-term projects that result in less frequent but more significant publications, and 8) a possible perception that specific findings do not add substantially to the existing body of knowledge, thereby choosing not to report them.

Concerning the publication of negative results, Heinl et al. suggested adopting a more accepted format called 'registered reports' in psychology. Under this format, a study plan is submitted to a journal before starting the research, it is then peer-reviewed and, if accepted, the results are guaranteed to be accepted irrespective of whether they are positive, negative or inconclusive. This could certainly be an option. However, it is balanced against concerns that some researchers may use the negative results to inflate their CV.

Although there could be situations where the results of negative experiments may be problematic, we believe that proper reporting of the hypotheses, experimental design and the execution of such experiments would help distinguish experiments with significant flaws from those underpowered or whose results appear to be truly negative. In this regard, positive and negative controls in the experiment help to identify experiments with execution problems that invalidate their conclusions.

Still, it is essential to acknowledge that the findings of this study are primarily based on self-reported impacts and impressions of the participants, which may differ from objectively measured outcomes. This reliance on subjective reports rather than quantifiable data could potentially influence the accuracy and generalizability of the results.

Now, it is the turn of legislators, funding agencies, institutions, scientific societies and ethical committees to provide practical ways to promote the publication of negative results. The mandate for data management and sharing plans represents a move towards greater openness in scientific research. However, these plans are not tailored specifically to animal research and, in practical terms, they are still in their infancy. Specific measures could be undertaken, like requiring registration of animal experiments before data collection and subsequent follow-up of the results, providing practical ways to publish negative results, or adopting appropriate incentives for the laboratory or individual researcher.

Medical research is well ahead of animal research concerning the publication of negative results. ¹⁰ Many relevant institutions have already recommended the need for reporting negative results of clinical trials: the International Committee of Medical Journal Editors, World Health Organization and Committee on Publication Ethics. ¹¹ Despite this strong support, it has also been an essential bias towards positive

results by scientific editors and researchers themselves. 11 The main difference between clinical trials and preclinical studies is probably in the mandatory requirement to register all clinical trials in centralized registries controlled by government agencies (e.g. clinicaltrials.gov in the case of the Food and Drug Administration, or clinicaltrialsregister.eu in the case of the European Medicines Agency). When compared with animal alternatives such as the Preclinicaltrials. eu, 12 animalstudyregistry.org, 13 we observe two important differences: 1) in clinical trials, there is an exhaustive tracking of the status of the trial (not yet recruiting, recruiting, withdrawn, completed, terminated, etc.) and the dates in which they change; 2) in clinical trials there is an explicit tracking of the outcome of the experiment either provided by the applicant or automatically matched by the agency through the registration numbers reported in scientific articles. Some stakeholders point to a potential drawback of preclinical registries, which is the possibility of scooping some studies and giving advantages to competitors. To address this concern, registries such as the OSF allow researchers to apply an embargo period during which the information in the registry is not made public or by making the information public after the consent of the main investigator. 14 This is not a problem in clinical trials because patents protect drugs.

Registries such as clinicaltrials.gov and clinicaltrials-register.eu currently hold 459,627 and 43,630 studies, respectively. Compared with their preclinical counterparts, at the time of writing, we see 149 registered studies in animalstudyregistry.org and 127 in preclinicaltrials.eu.

This difference is even more striking if we consider that many preclinical studies never reach the clinical stage. The discrepancy can be attributed to two main factors. First, registering clinical trials has been established for a more extended period compared with preclinical studies. Second, the registration of clinical trials is mandatory, whereas it remains voluntary for preclinical studies. Despite the potential impact of animal registries^{1,14,15} on improving many aspects of preclinical animal research, after four years of experience, they have not yet had any significant impact.

In summary, we believe that the four keys to improving the culture of sharing negative results in preclinical research with animals are: 1) the obligation to preregister studies, 2) a thorough tracking of their status, 3) of their results, and 4) a realistic way of publishing negative results. Despite the possible inconveniences and drawbacks of such a practice, achieving this would result in important scientific, ethical and economic benefits for society and science.

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Data availability

The anonymized data and a summary of the results are publicly available on the Open Science Framework, https://osf.io/9p7kz/.

Declaration of conflicting interests

The authors have no conflicts of interest to declare.

Ethical approval

This paper does not contain data obtained from animals. It describes the results of a survey of researchers working with animals. Our survey was approved by the Spanish National Research Council's (CSIC) Ethics Committee before commencement.

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Avis des chercheurs utilisant des animaux sur la publication de résultats négatifs et les adoptions de politiques subséquentes

Résumé

Depuis plus d'une décennie, la non-publication des résultat négatifs issus des études précliniques est identifiée comme une préoccupation importante dans la recherche biomédicale. Une telle sous-déclaration est considérée comme un facteur jouant un rôle dans la crise de reproductibilité sur le terrain et a été reconnue par des revues importantes comme Science and Nature. En réponse aux taux constamment élevés de non-publication de la recherche animale préclinique en Europe, une enquête a été menée auprès de la communauté de la recherche biomédicale pour recueillir les points de vue des chercheurs sur la publication de résultats négatifs. Grâce à la plateforme EUSurvey, plus de 200 chercheurs travaillant directement avec des animaux ont été interrogés. L'étude visait à comprendre la fréquence des résultats négatifs, les raisons de leur non-publication et les avantages et inconvénients perçus de la publication de ces résultats. Les enseignements tirés de l'enquête pourraient guider les étapes vers la promotion de la transparence

scientifique, le raffinement des méthodologies de recherche, la réduction de l'utilisation d'animaux dans les expériences et la réduction des déchets de recherche.

Ansichten von Tierforschern über die Veröffentlichung negativer Ergebnisse und daraufhin ergriffene Maßnahmen

Abstract

Seit über einem Jahrzehnt gilt die Nichtveröffentlichung negativer Ergebnisse aus präklinischen Studien als großes Problem in der biomedizinischen Forschung. Diese unzureichende Berichterstattung wird als eine Ursache für die Reproduzierbarkeitskrise in diesem Bereich erachtet und wurde von bedeutenden Fachzeitschriften wie Science und Nature bestätigt. Als Reaktion auf die konstant hohen Raten der Nichtveröffentlichung präklinischer Tierversuche in Europa wurde eine Umfrage unter biomedizinischen Forschern durchgeführt, um ihre Meinung zur Veröffentlichung negativer Ergebnisse zu erfahren. Mithilfe der EUSurvey-Plattform wurden über 200 Forscher, die direkt mit Tieren arbeiten, befragt. Ziel der Untersuchung war es, die Häufigkeit negativer Ergebnisse, die Gründe für deren Nichtveröffentlichung sowie die Vor- und Nachteile der Veröffentlichung solcher Ergebnisse zu ermitteln. Die Erkenntnisse aus der Umfrage könnten dazu beitragen, Transparenz in der Wissenschaft zu fördern, Forschungsmethoden zu verbessern, den Einsatz von Tieren in Versuchen zu verringern und sog. Forschungsabfall zu minimieren.

La opinión de los investigadores de animales sobre la publicación de resultados negativos y la adopción de políticas posteriores

Resumen

Durante más de una década, la no publicación de resultados negativos de estudios preclínicos ha sido identificada como una preocupación significativa en la investigación biomédica. Esta falta de publicación se considera un factor que contribuye a la crisis de reproducibilidad en el campo y ha sido reconocida por revistas importantes como Science y Nature. En respuesta a las consistentemente altas tasas de no publicación de investigaciones preclínicas con animales en Europa, se realizó una encuesta entre la comunidad de investigación biomédica para recopilar sus opiniones sobre la publicación de resultados negativos. Utilizando la plataforma EUSurvey, se encuestó a más de 200 investigadores que trabajan directamente con animales. El estudio trataba de conocer la frecuencia de los resultados negativos, las razones de su no publicación y las ventajas y desventajas percibidas respecto a hacer públicos dichos resultados. Los conocimientos obtenidos de la encuesta podrían guiar los pasos hacia la promoción de la transparencia en la ciencia, la mejora de las metodologías de investigación, la reducción del uso de animales en los experimentos y la minimización del desperdicio en la investigación.

Appendix 1. Demographics

Leading (29%), established (32%), early (19%)	Proportion ne Decided not to
Academic (74%), Government (20%)	Unable to pub
Spain (26%), Germany (14%), Ireland	Published
(9%), Switzerland (8%)	Sharing negat
Female (60%), male (40%)	should be p
0-10 (38%), 11-20 (21%)	
0-10 (45%), 10-20 (25%)	
Mice (80%), rats (46%), rabbits and ferrets (11%), fishes (9%)	I would benef researchers
No (73%), don't know what preregistration is (19%)	negative res
	early (19%) Academic (74%), Government (20%) Spain (26%), Germany (14%), Ireland (9%), Switzerland (8%) Female (60%), male (40%) 0–10 (38%), 11–20 (21%) 0–10 (45%), 10–20 (25%) Mice (80%), rats (46%), rabbits and ferrets (11%), fishes (9%) No (73%), don't know what

Research experience

2) valuable knowledge	Proportion negative results	32%
Published 25% Sharing negative results should be promoted 1) avoid repetition (49%) 2) valuable knowledge (39%), 3) reduction (32% 1 would benefit from other researchers'	Decided not to publish	38%
Sharing negative results should be promoted 1) avoid repetition (49%) 2) valuable knowledge (39%), 3) reduction (32% 87% 87%	Unable to publish	20%
should be promoted 1) avoid repetition (49%) 2) valuable knowledge (39%), 3) reduction (32%) 1 would benefit from other researchers'	Published	25%
2) valuable knowledge (39%), 3) reduction (32% researchers' 87%	Sharing negative results	95%, because:
researchers'	should be promoted	1) avoid repetition (49%), 2) valuable knowledge (39%), 3) reduction (32%)
	researchers'	87%

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Causes of negative results

True lack of effect	90%
Variability	80%
Low sample size	68%
Animal or environmental factors	66%
Unknown reasons	49%
Random chance	38%
Poor execution	38%
Poor hypotheses	35%
Poor compliance to guidelines	31%

Reasons for unpublished negative results

Low success	96%
Lack of culture	84%
Absence of journal	78%
Low number of citations	72%
No incentive	67%
They cannot decide to publish	66%
Afraid of showing negative results	59%
Unwilling to go a full peer-review	58%
Not obliged	54%
Afraid of bad design	54%
Not useful	52%
Not enough time	51%
Unsure whether truly negative	49%
Pressure from collaborators not to publish	42%
Legal constraints	18%

Policies governing sharing of negative results

97%
78%
75%
50%
38%
37%
34%

How to publish negative results

Easy discoverability	89%
Can be cited	80%
Quality control before publishing	79%
Easy to navigate and submit	78%
Free to publish	77%
Full paper in peer-reviewed journal	70%
Hosted by recognized institution	66%
Peer-review control	58%
Free-style non-peer-reviewed repository	57%
Allows comments	57%
Open science database	52%

Problems of publishing negative results

Fake submissions in a non-peer-review site	73%
Low quality if not peer-reviewed	70%
Still, some experiments would be repeated	58%
CV inflation	56%
Not used	10%

Benefits of publishing negative results

Important savings	91%
Publicly funded projects should always report	87%
Societal benefits	84%
Participants want results published	74%
Unethical not to publish	67%
Better future hypotheses and experiments	49%
Avoid repetition of experiments	38%
Economical and time benefits	25%
Reduction of animals	12%
Reduction of publication bias	11%

Supplementary Material

This supplementary material shows the call to participate in the survey, all the survey questions and some very simple statistical summary of each question. 237 researchers replied to the survey between November 29th, 2021 and January 6th, 2022. About 60% of the respondents were established or leading researchers. Also, 60% of them were female. About 75% of them worked at academic institutions. About 95% of the respondents worked at European countries. Respondents have published an average of 47 scientific articles and have been working, on average, 16 years with animals.

Call to participate in the survey

Animal researchers' views on the sharing of null and negative results

We, researchers at the <u>Spanish National Research Council (CSIC)</u>, the <u>University Carlos III of Madrid</u>, Spain, and the <u>University of Melbourne</u>, Australia, are currently researching how animal researchers design, analyse, interpret and communicate the findings of their research.

As part of this research, we are inviting **animal researchers** from around the world to participate in a survey to share their experiences with, and views on, the sharing of research data, particularly from experiments that observed **null** or **negative** results. Please, fill this survey if your research involves working with animals.

The survey should take a few minutes to complete, and we would like to collect all the responses before Christmas 2021. We greatly appreciate your time and help with this project.

Yours sincerely, Dr. Carlos Oscar Sorzano

(This survey was approved by the ethical committee of CSIC.)

Results

Demographics I

Thank you for agreeing to participate in the survey. Before we begin we would like to ask you a few questions about yourself and your research experience.

Career status

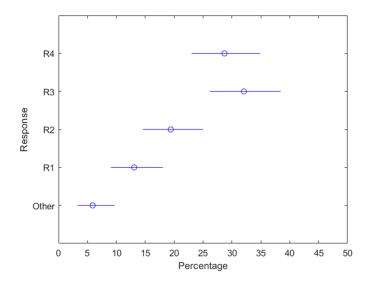
R1: Student researcher (receiving research training up to the point of PhD) (13.1%)

R2: Early researcher (researchers whose work is unfunded or funded by others' grants) (19.4%)

R3: Established researcher (researchers whose work is salaried, or partially or fully funded by grants they have received) (32.1%)

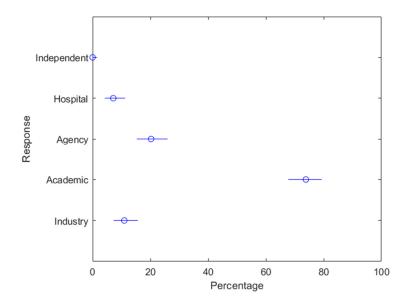
R4: Leading Researcher (researchers leading their research area or field with grants that fund others' research) (28.7%)

Other, (please, describe) (5.9%). Within this group, the only subgroup above 1% was the one of veterinarians (2.1%).



What sector does the organisation that supports your research belong to? (Select all that apply)

- a. Industry (biopharmaceutical company, biotech company) (11.0%)
- b. Non-industry (academic institution) (73.8%)
- c. Non-industry (hospital setting) (7.2%)
- d. Non-industry (government agencies, non-government agency) (20.3%)
- e. Independent researcher (0%)
- f. Other (0%)



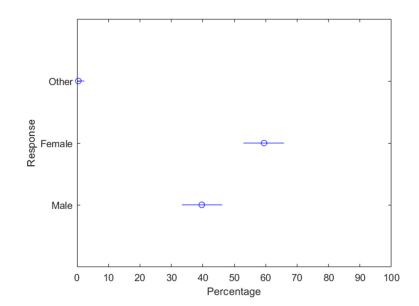
What is your primary country of work?

Spain	62
Germany	33
Ireland	21
Switzerland	20
Portugal	14
Belgium	12
United Kingdom	12
Denmark	11
Netherlands	9
United States of America	9
France	8
Slovenia	6
Italy	3
Croatia	2
Finland	2
Greece	2
Sweden	2
Austria	1
Georgia	1
Iran	1
Japan	1
Norway	1
Poland	1

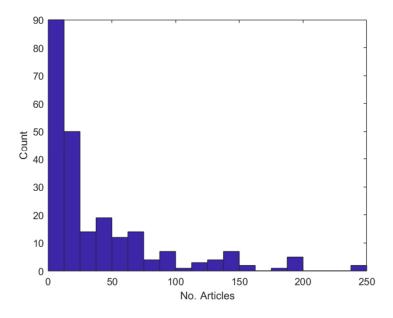
Romania 1
Saint Kitts and Nevis 1

What is your gender?

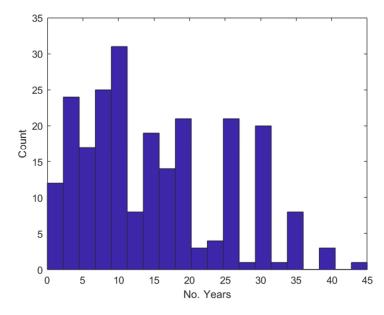
- a. Male (39.7%)
- b. Female (59.5%)
- c. None of the above (0.4%)



Demographics II Approximately, how many scientific articles have you authored over your career?



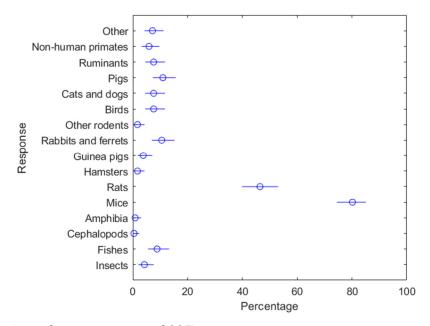
Approximately, how many years have you been using animals for scientific purposes as part of your research?



.

What kind of animals do you normally work with? (Select all that apply.)

- a. Insects (4.2%)
- b. Fishes (8.9%)
- c. Cephalopods (0.4%)
- d. Amphibia (0.8%)
- e. Mice (80.2%)
- f. Rats (46.4%)
- g. Hamsters (1.7%)
- h. Guinea pigs (3.8%)
- i. Rabbits and ferrets (10.5%)
- j. Other rodents (1.7%)
- h. Birds (7.6%)
- j. Cats and dogs (7.6%)
- k. Pigs (11.0%)
- 1. Ruminants (7.6%)
- m. Non-human primates (5.9%)
- n. Other (7.2%)



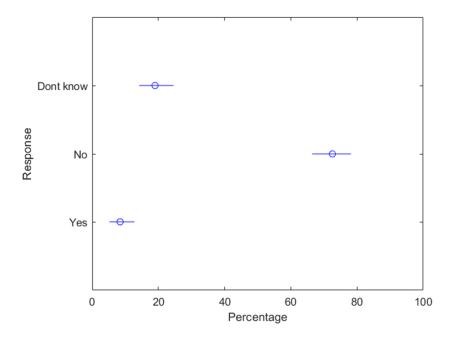
Other species (no. of responses, out of 237):

Horses	4
Lizards	3
Reptiles	2
Mollusks	2
Donkeys	1
Wolves	1

Have you ever pre-registered a protocol for one of your studies? (i.e. posted a study protocol in a public registry

(e.g. <u>www.animalstudyregistry.org</u>, <u>www.preclinicaltrials.eu</u> or <u>www.osf.io/registries</u>) before collecting data)

- a. Yes (8.4%)
- b. No (72.6%)
- c. Don't know what 'pre-registration' is (19.0%)



Definitions for the Survey

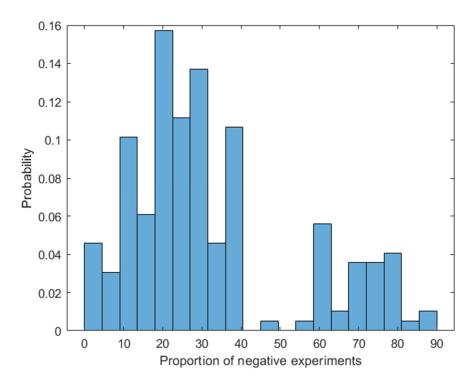
The remainder of this survey will ask you for your views on <u>negative results</u>, and the <u>research</u> <u>data</u> from <u>negative experiments</u> that used animal research subjects.

For the purposes of this survey we will abide by the following definitions of these terms:

- Research data is defined as information collected at the level of the subject of research (e.g. animal, tissue sample) that would theoretically enable others to verify or regenerate any of your published findings.
- A <u>negative result</u> as the outcome of a statistical test demonstrating no statistically significant difference or association with respect to a reference group, or an effect size so small as to be of no practical importance. These negative results may be reported as part of a larger experiment in which other positive results are reported.
- A <u>negative experiment</u> is a collection of assays whereby either: the main findings, or most of the findings are <u>negative results</u>. Negative experiments should be distinguished from the larger set of <u>unreported experiments</u>, in which a whole set of essays remains unreported for whichever reason (e.g. journal rejections, paper never written, primary researcher left research institution/passed away)

Research experience I

What proportion of all <u>your</u> animal research experiments to date do you think were <u>negative experiments</u>? (0-100%)

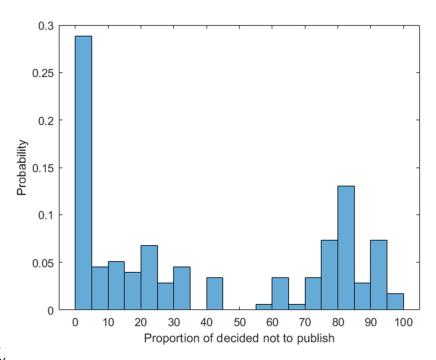


Mean = 32.2%

Of the estimated number of your negative experiments, approximately what proportion

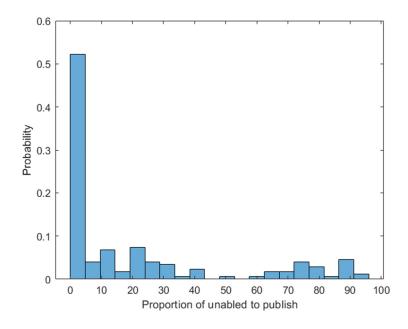
...

Did you decide not to try to publish? (0-100%)

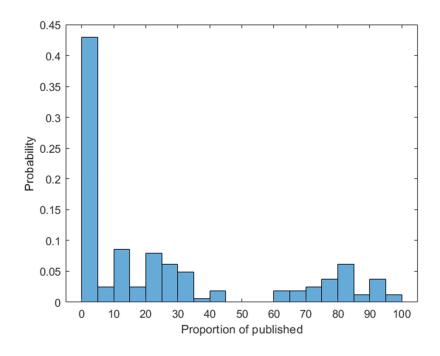


Mean = 38.2%

Were you unable to publish? (0-100%)

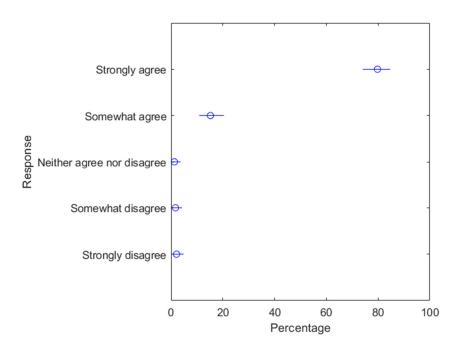


Mean=19.7%
Were you able to publish? (0-100%)



Perceptions on negative data I

How much do you agree or disagree with the following statement? "The animal research community should promote and facilitate the sharing of the research data or reports from negative experiments."



Strongly agree: 79.8% Somewhat agree: 15.2%

Neither agree nor disagree: 1.3%

Somewhat disagree: 1.7% Strongly disagree: 2.1%

Why? Please, briefly explain your answer

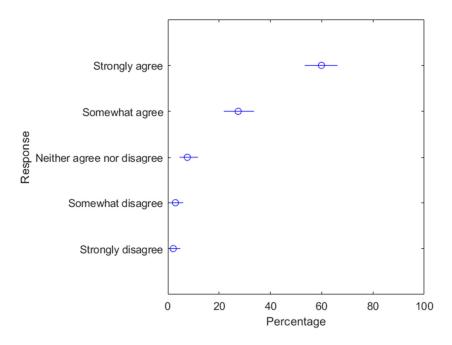
93.4% of the researchers had a positive attitude about sharing negative results. The main reasons were:

- Avoiding repetitions of experiments (focusing in their time and money considerations): 49.2%
- Obtaining valuable scientific knowledge: 39.1%
- Reducing the number of animals: 32.0%
- Allowing better design of future experiments: 10.7%
- Ethical considerations towards animals or society: 9.1%
- Reducing the publication bias: 8.1%

10.2% of the researchers raised some concerns about the design or the execution of the experiment, its statistical analysis, or the usefulness of having negative results available.

It must be noted that these categories are not mutually exclusive. For example, one researcher may be in favor of sharing negative results for multiple reasons and, at the same time, raise concerns about the fact that a negative result is achieved simply by an incorrect execution of the experiment.

How much do you agree or disagree with the following statement? "My research would benefit from greater sharing of the research data from negative experiments."



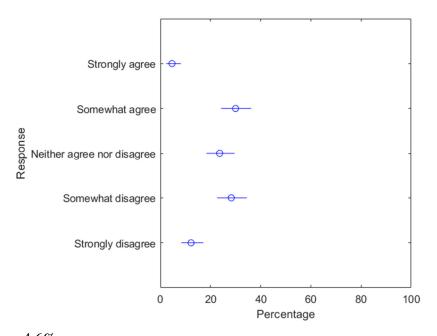
Strongly agree: 59.9% Somewhat agree: 27.4%

Neither agree nor disagree: 7.6%

Somewhat disagree: 3.0% Strongly disagree: 2.1%

Perceptions on negative data II. What are, in your opinion, the key causes for negative results?

Poorly defined hypotheses

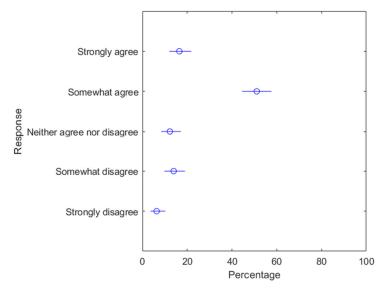


Strongly agree: 4.6% Somewhat agree: 30.0%

Neither agree nor disagree: 23.6%

Somewhat disagree: 28.3% Strongly disagree: 12.2%

Low sample size

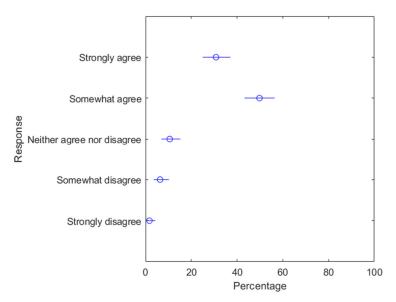


Strongly agree: 16.5% Somewhat agree: 51.1%

Neither agree nor disagree: 12.2%

Somewhat disagree: 13.9% Strongly disagree: 6.3%

Variability of the observed variables



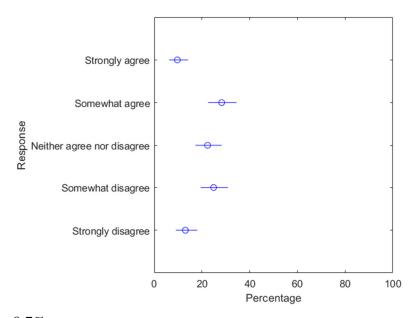
Strongly agree: 30.8%

Somewhat agree: 49.8%

Neither agree nor disagree: 10.5%

Somewhat disagree: 6.3% Strongly disagree: 1.7%

Poorly performed experiments

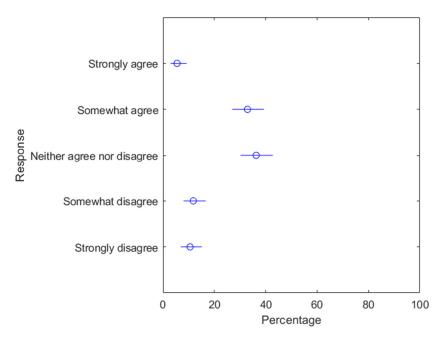


Strongly agree: 9.7% Somewhat agree: 28.3%

Neither agree nor disagree: 22.4%

Somewhat disagree: 24.9% Strongly disagree: 13.1%

Random chance

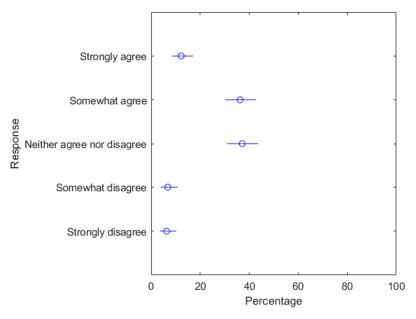


Strongly agree: 5.4% Somewhat agree: 32.9%

Neither agree nor disagree: 36.3%

Somewhat disagree: 11.8% Strongly disagree: 10.5%

Unknown reasons

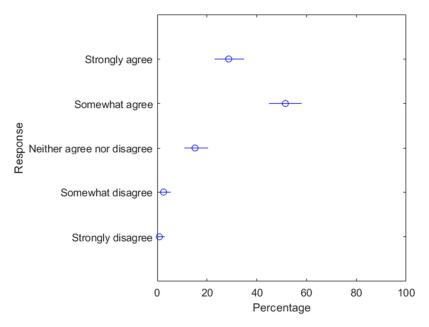


Strongly agree: 12.2% Somewhat agree: 36.3%

Neither agree nor disagree: 37.1%

Somewhat disagree: 6.8% Strongly disagree: 6.3%

True lack of correlations or differences between groups

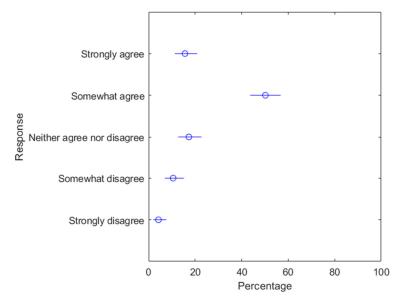


Strongly agree: 28.7% Somewhat agree: 51.5%

Neither agree nor disagree: 15.2%

Somewhat disagree: 2.5% Strongly disagree: 0.8%

Animal or environmental factors

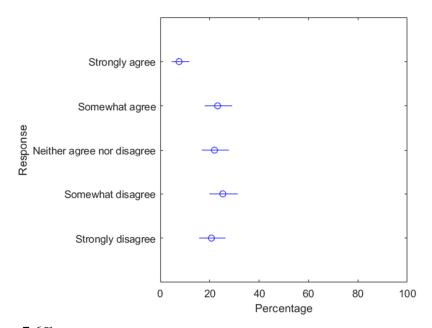


Strongly agree: 15.6% Somewhat agree: 50.2%

Neither agree nor disagree: 17.3%

Somewhat disagree: 10.5% Strongly disagree: 4.2%

Poor compliance with guidelines or recommendations



Strongly agree: 7.6% Somewhat agree: 23.2%

Neither agree nor disagree: 21.9%

Somewhat disagree: 25.3% Strongly disagree: 20.7%

Please, list any other key causes for negative results

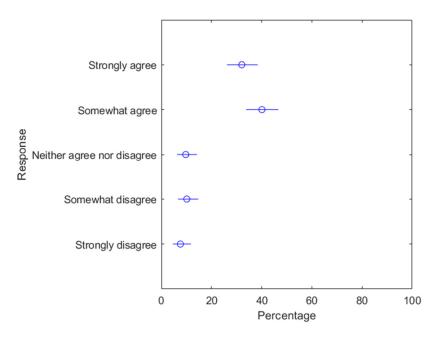
The following items have been mentioned as the main other causes for negative results:

- Execution/methodological/procedural issues related to the animal handling or experimental equipment: 34.6%
- Experimental design, especially those aspects related to the control of other variables: 32.7%
- Biological variability, especially when going from in vitro to in vivo experiments: 26.9%
- Underpowered experiments due to a small sample size: 19.2%
- Incorrect selection of the animal model: 17.3%
- Poor statistical analysis: 9.6%
- Publication pressure: 5.8%

It must be noted that reasons are not mutually exclusive and a researcher may indicate multiple reasons. This makes that the percentages above do not have to add up to 100%.

Perceptions on negative data III. Why do you think researchers do not typically publish their negative experiments?

The belief that papers presenting negative results do not get a high number of citations



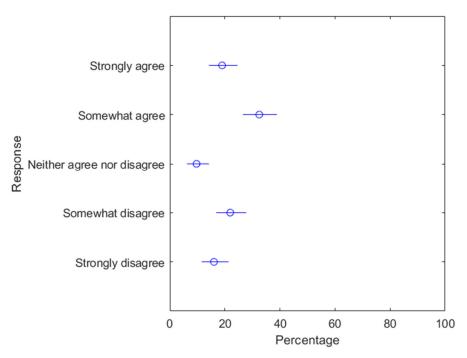
Strongly agree: 32.1% Somewhat agree: 40.1%

Neither agree nor disagree: 9.7%

Somewhat disagree: 10.1%

Strongly disagree: 7.6%

The belief that negative results are not so useful

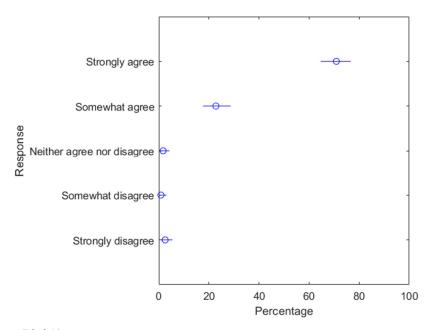


Strongly agree: 18.9% Somewhat agree: 32.5%

Neither agree nor disagree: 9.7%

Somewhat disagree: 21.9% Strongly disagree: 16.3%

A lack of culture of publishing negative experiments

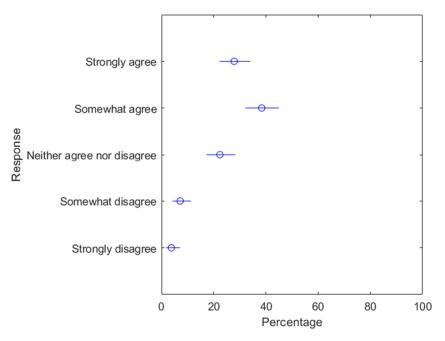


Strongly agree: 70.9% Somewhat agree: 22.8%

Neither agree nor disagree: 1.7%

Somewhat disagree: 0.8% Strongly disagree: 2.5%

The decision to publish them is not in their hands

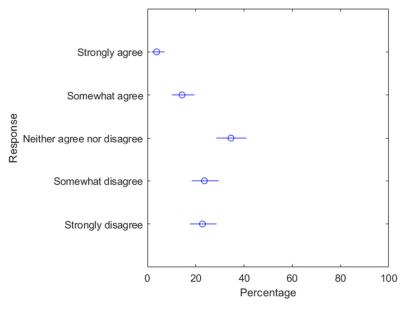


Strongly agree: 27.8% Somewhat agree: 38.4%

Neither agree nor disagree: 22.4%

Somewhat disagree: 7.2% Strongly disagree: 3.8%

Legal constraints/Problems with intellectual property

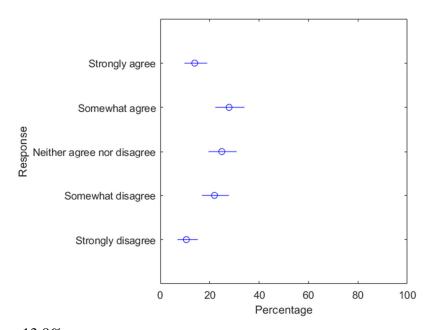


Strongly agree: 3.8% Somewhat agree: 14.3%

Neither agree nor disagree: 34.6%

Somewhat disagree: 23.6% Strongly disagree: 22.8%

Pressure from collaborators not to publish

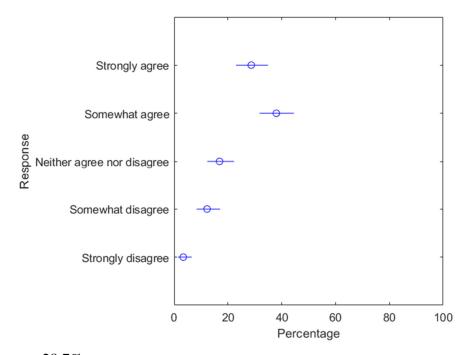


Strongly agree: 13.9% Somewhat agree: 27.8%

Neither agree nor disagree: 24.9%

Somewhat disagree: 21.9% Strongly disagree: 10.5%

They do not have any incentive to do so

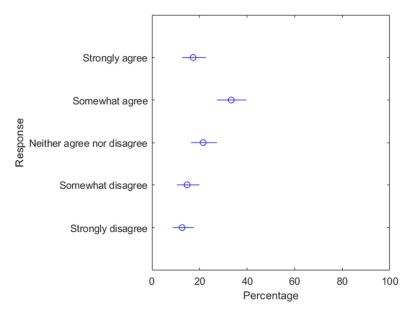


Strongly agree: 28.7% Somewhat agree: 38.0%

Neither agree nor disagree: 16.9%

Somewhat disagree: 12.2% Strongly disagree: 3.4%

They do not have the time to do so

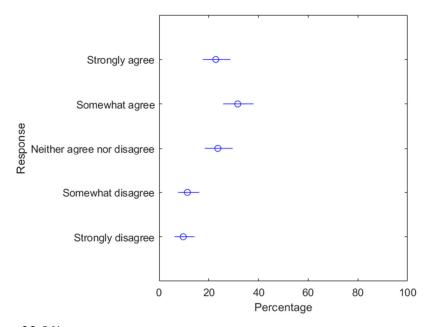


Strongly agree: 17.3% Somewhat agree: 33.3%

Neither agree nor disagree: 21.5%

Somewhat disagree: 14.8% Strongly disagree: 12.7%

They are not obliged

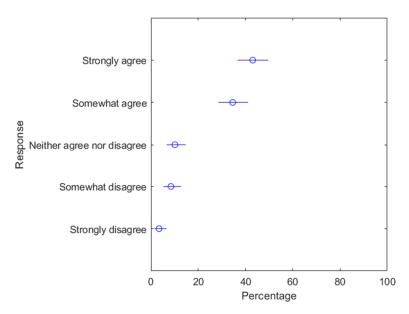


Strongly agree: 22.8% Somewhat agree: 31.6%

Neither agree nor disagree: 23.6%

Somewhat disagree: 11.4% Strongly disagree: 9.7%

There is no realistic place to publish negative experiments

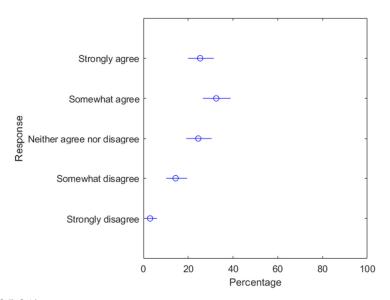


Strongly agree: 43.0% Somewhat agree: 34.6%

Neither agree nor disagree: 10.1%

Somewhat disagree: 8.4% Strongly disagree: 3.4%

They do not want to go through a full peer-reviewed process as for a regular paper with positive results

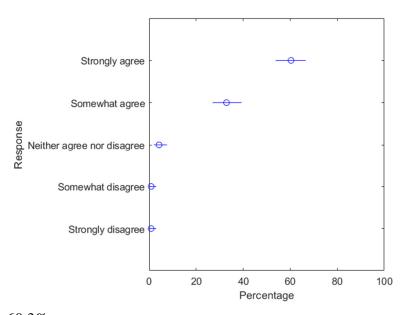


Strongly agree: 25.3% Somewhat agree: 32.5%

Neither agree nor disagree: 24.5%

Somewhat disagree: 14.3% Strongly disagree: 3.0%

They think the likelihood of successfully publishing the results of negative experiments is very low

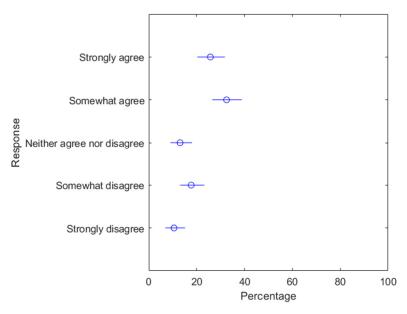


Strongly agree: 60.3% Somewhat agree: 32.9%

Neither agree nor disagree: 4.2%

Somewhat disagree: 0.8% Strongly disagree: 0.8%

They are afraid of showing that they failed to obtain positive results

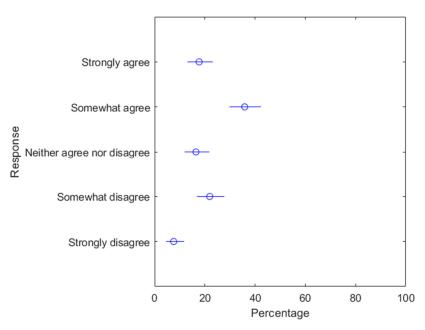


Strongly agree: 25.7% Somewhat agree: 32.5%

Neither agree nor disagree: 13.1%

Somewhat disagree: 17.7% Strongly disagree: 10.5%

They are afraid of showing that they have tried an experiment that others might consider useless from the very beginning

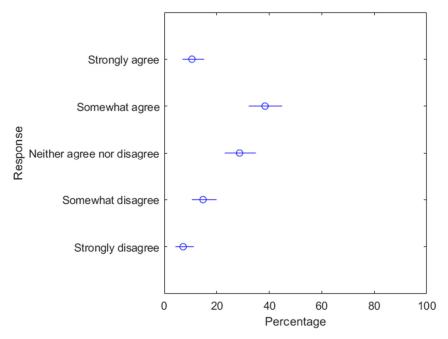


Strongly agree: 17.7% Somewhat agree: 35.9%

Neither agree nor disagree: 16.5%

Somewhat disagree: 21.9% Strongly disagree: 7.6%

They are not sure if their results are truly negative



Strongly agree: 10.5% Somewhat agree: 38.4%

Neither agree nor disagree: 28.7%

Somewhat disagree: 14.8% Strongly disagree: 7.2%

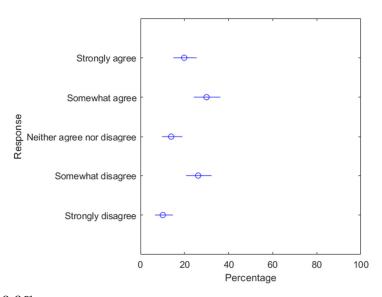
Other reasons: (please, describe)

The following reasons have been put forward as to why negative results are not published:

- Journals do not accept, in general, negative results: 44.0%
- Publication of negative results may negatively affect future grants from funding agencies and companies: 20%
- Researchers cannot explain the reasons for the negative results, so they are unsure to publish them: 20%
- Researchers cannot interpret correctly the meaning of the negative results: 20%
- Experiments yielding negative results are seen as intermediate experiments leading to a better design: 16%

Policies governing sharing of negative results. How much do you agree or disagree with the following statements?

Researchers are free to decide whether to share the results from negative experiments or not

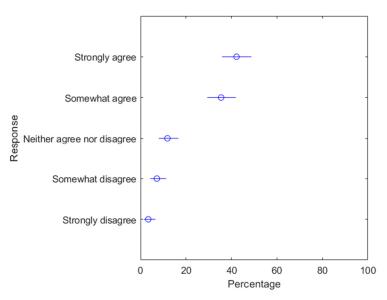


Strongly agree: 19.8% Somewhat agree: 30.0%

Neither agree nor disagree: 13.9%

Somewhat disagree: 26.2% Strongly disagree: 10.1%

<u>Funders</u> should require that all results obtained with their money should be made available (either through the standard publication channels or through alternative avenues)

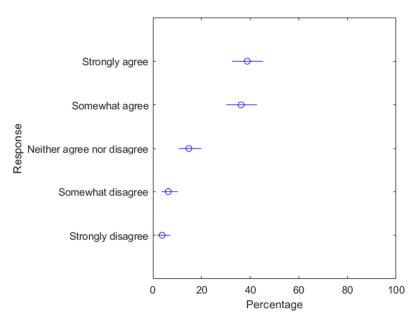


Strongly agree: 42.2% Somewhat agree: 35.4%

Neither agree nor disagree: 11.8%

Somewhat disagree: 7.2% Strongly disagree: 3.4%

<u>Institutions</u> should require that all results obtained within their facilities should be made available (either through the standard publication channels or through alternative avenues)

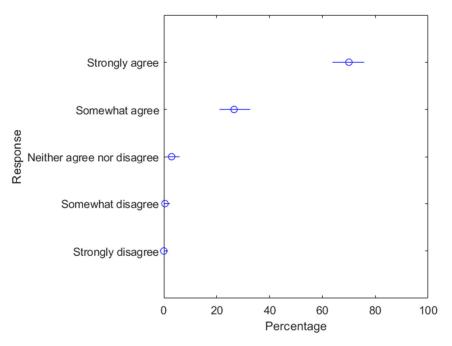


Strongly agree: 38.8% Somewhat agree: 36.3%

Neither agree nor disagree: 14.8%

Somewhat disagree: 6.3% Strongly disagree: 3.8%

<u>Scientific societies</u> should promote the sharing of the data from negative experiments

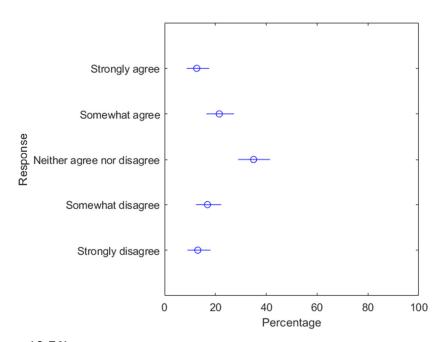


Strongly agree: 70.0% Somewhat agree: 26.6%

Neither agree nor disagree: 3.0%

Somewhat disagree: 0.4% Strongly disagree: 0%

Part of the evaluation of a researcher comes from the number of datasets from negative experiments that they have shared

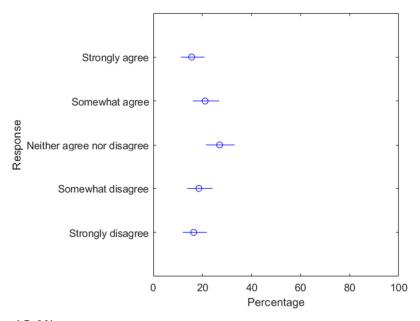


Strongly agree: 12.7% Somewhat agree: 21.5%

Neither agree nor disagree: 35.0%

Somewhat disagree: 16.9% Strongly disagree: 13.1%

Laboratories are rewarded for sharing the data from negative experiments

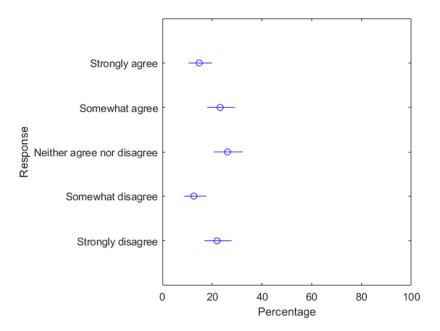


Strongly agree: 15.6% Somewhat agree: 21.1%

Neither agree nor disagree: 27.0%

Somewhat disagree: 18.6% Strongly disagree: 16.5%

Individual researchers are rewarded for sharing the data from negative experiments



Strongly agree: 14.8% Somewhat agree: 23.2%

Neither agree nor disagree: 26.2%

Somewhat disagree: 12.7% Strongly disagree: 21.9%

Which rewards are appropriate for a laboratory?

The following rewards have been mentioned:

• Better access to funding: 36.9%

None: 24.3%

• Being able to publish negative results: 22.3%

Reputation/Recognition: 15.5%

• Better access to animal facilities and equipment: 6.8%

Which rewards are appropriate for a researcher?

The following rewards have been mentioned:

Reputation/Recognition: 34.3%

Being able to publish negative results: 31.4%

• Better access to funding: 28.4%

• None: 11.8%

Sharing negative results I

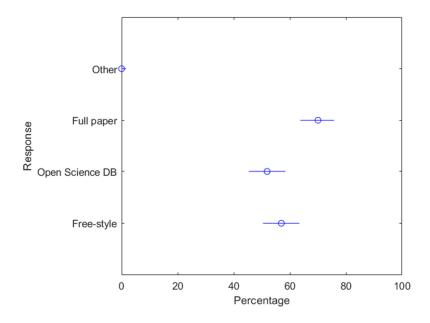
In which way would you be willing to share the findings of your negative experiments? (Select all that apply)

A free-style report submitted to a non-peer reviewed repository (like, arXiv, bioRxiv, ... but dedicated to negative results in animal experiments): 57.0%

Uploading raw data and a small report to some Open Science database: 51.9%

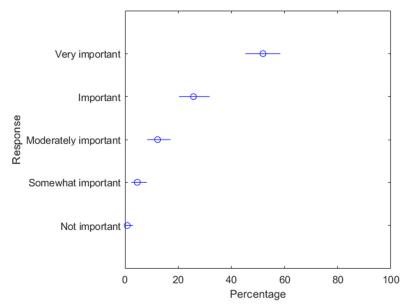
Writing a full paper and submitting to a peer reviewed journal: 70.0%

Others (please, specify): 0.0%



If you were considering submitting your results from a negative experiment to a non-peer reviewed repository, how important would the following characteristics be? (assess all of them from 1="Not important" to 5="Extremely important")

The repository is easy to navigate and submit

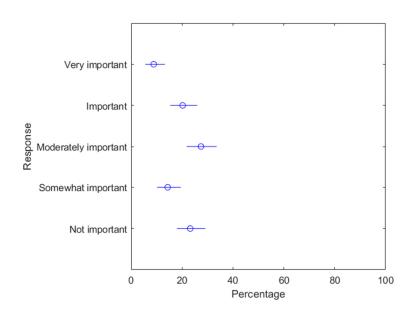


Very important: 51.9% Important: 25.7%

Moderately important: 12.2% Somewhat important: 4.6%

Not important: 0.8%

Part of the evaluation of a researcher comes from the number of datasets from negative experiments that they have shared

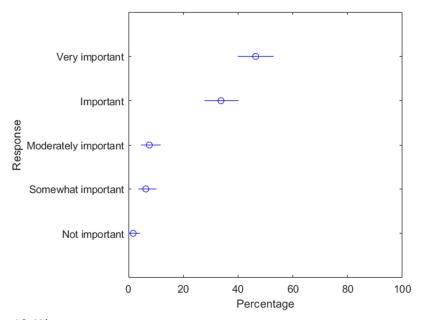


Very important: 8.9% Important: 20.2%

Moderately important: 27.4% Somewhat important: 14.3%

Not important: 23.2%

It can be cited as a scientific result

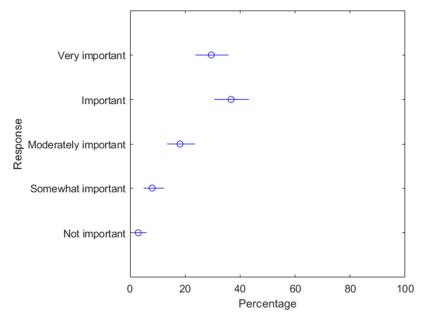


Very important: 46.4% Important: 33.8%

Moderately important: 7.6% Somewhat important: 6.3%

Not important: 1.7%

It is hosted at a recognized institution

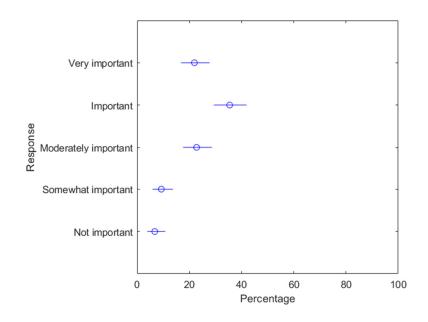


Very important: 29.5% Important: 36.7%

Moderately important: 18.1% Somewhat important: 8.0%

Not important: 3.0%

It allows comments from other users

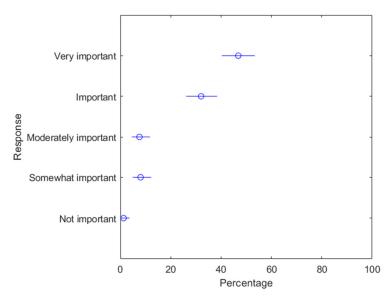


Very important: 21.9% Important: 35.4%

Moderately important: 22.8% Somewhat important: 9.3%

Not important: 6.8%

There is a quality control before making the report public



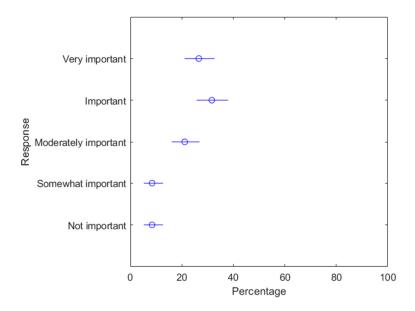
Very important: 46.8%

Important: 32.1%

Moderately important: 7.6% Somewhat important: 8.0%

Not important: 1.3%

There should be a rigorous peer-review before making the results public

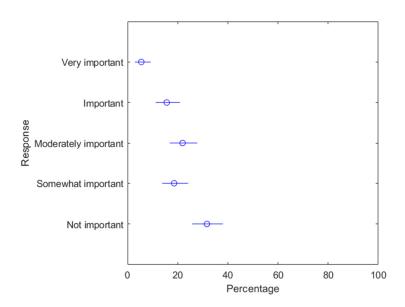


Very important: 26.6% Important: 31.6%

Moderately important: 21.1% Somewhat important: 8.4%

Not important: 8.4%

No submission is rejected



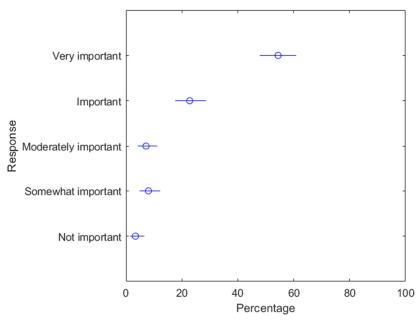
Very important: 5.5%

Important: 15.6%

Moderately important: 21.9% Somewhat important: 18.6%

Not important: 31.6%

It is free

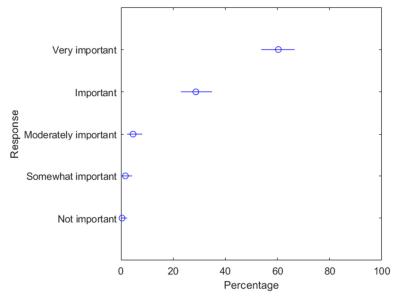


Very important: 54.4% Important: 22.8%

Moderately important: 7.2% Somewhat important: 8.0%

Not important: 3.4%

It is easy for others to discover



Very important: 60.3% Important: 28.7%

Moderately important: 4.6% Somewhat important: 1.7%

Not important: 0.4%

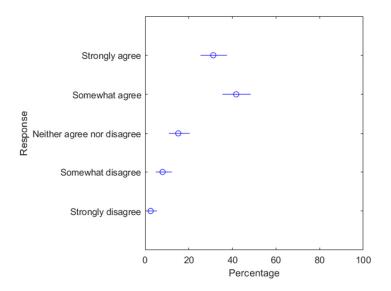
Others: (please, describe)

The following characteristics have been mentioned:

- It should be peer-reviewed: 50%
- It should request raw data: 21.4%
- The publication process should be easy: 21.4%

Sharing negative results II. Problems/caveats.

A non-peer reviewed repository could be flooded with fake submissions from interested agents (fundamentalists of animal rights, ...)

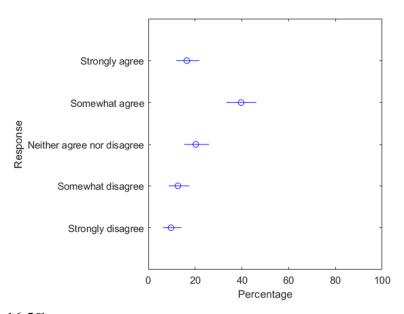


Strongly agree: 31.2% Somewhat agree: 41.8%

Neither agree nor disagree: 15.2%

Somewhat disagree: 8.0% Strongly disagree: 2.5%

Some researchers could use publications of negative experiments as a way to inflate their own CV



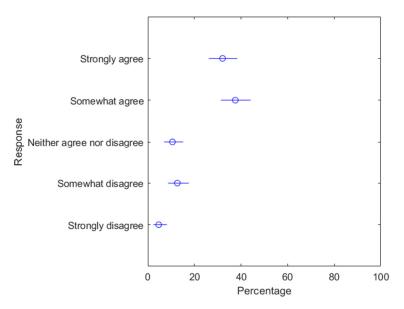
Strongly agree: 16.5% Somewhat agree: 39.7%

Neither agree nor disagree: 20.3%

Somewhat disagree: 12.7%

Strongly disagree: 9.7%

If it is easy to publish negative experiments, then most negative results publications or reports will be useless due to low-quality description caused by the lack of peer review

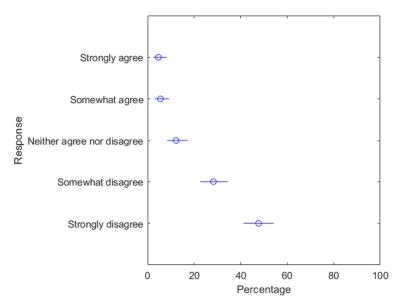


Strongly agree: 32.1% Somewhat agree: 37.6%

Neither agree nor disagree: 10.5%

Somewhat disagree: 12.7% Strongly disagree: 4.6%

I would not search for negative experiments before starting my own research experiments

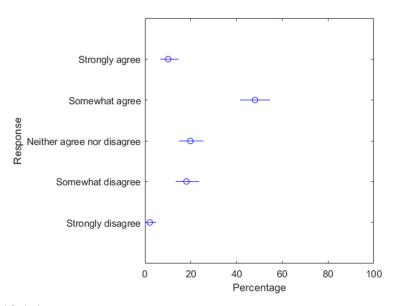


Strongly agree: 4.6% Somewhat agree: 5.5%

Neither agree nor disagree: 12.2%

Somewhat disagree: 28.3% Strongly disagree: 47.7%

Even if I saw a negative result in an experiment similar to mine, I would still try because there might be differences between the setup of my experiment and theirs



Strongly agree: 10.1% Somewhat agree: 48.1%

Neither agree nor disagree: 19.8%

Somewhat disagree: 18.1% Strongly disagree: 2.1%

How would Science benefit from the availability of the negative results?

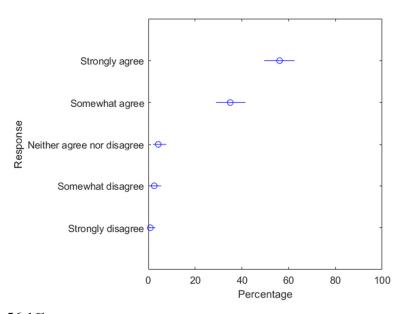
95% of the respondents see positive results in sharing negative results, while 4% see difficulties or doubt about its usefulness. The main reasons argued in favor of sharing negative results were:

- Better hypotheses formulation and design of future experiments: 49%
- Avoid repetition of experiments: 38%
- Economical and time benefits of better designed experiments or not repeating experiments: 25%
- Reduction of animals: 12%
- Reduction of the publication bias and benefits for metaanalyses: 11%
- Useful for educational purposes: 3%

Conclusions

How much do you agree with the following statements?

From the point of view of the funders, the publication of negative experiments could result in important savings thanks to avoiding repeating unsuccessful experiments

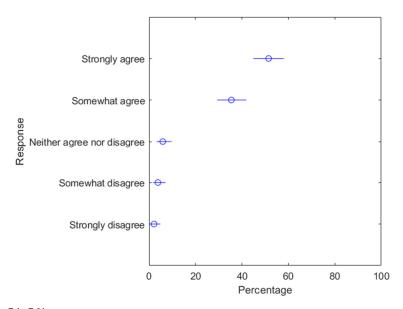


Strongly agree: 56.1% Somewhat agree: 35.0%

Neither agree nor disagree: 4.2%

Somewhat disagree: 2.5% Strongly disagree: 0.8%

All experiments funded with public money should be made public, independent of whether they are positive or negative, and the scientific publication channel (which may reject manuscripts)

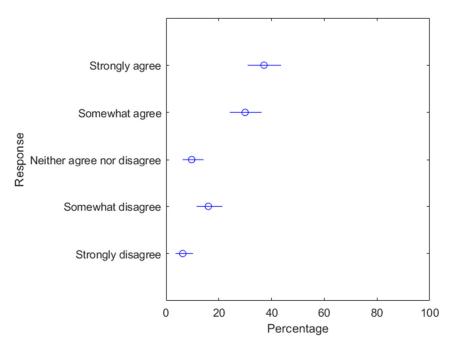


Strongly agree: 51.5% Somewhat agree: 35.4%

Neither agree nor disagree: 5.9%

Somewhat disagree: 3.8% Strongly disagree: 2.1%

From the point of view of animal welfare, it is unethical to repeat an experiment that somebody in the world has already done and found to be negative

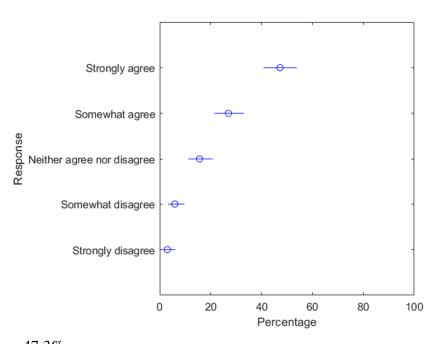


Strongly agree: 37.1% Somewhat agree: 30.0%

Neither agree nor disagree: 9.7%

Somewhat disagree: 16.0% Strongly disagree: 6.3%

I would not participate in a clinical trial if the experimenter decided not to publish the findings if they were found to be negative

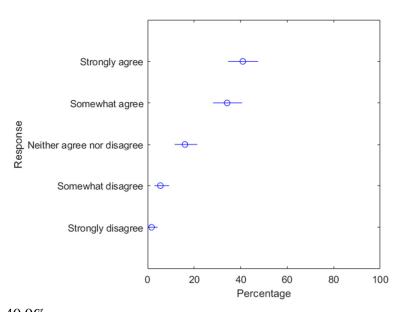


Strongly agree: 47.3% Somewhat agree: 27.0%

Neither agree nor disagree: 15.6%

Somewhat disagree: 5.9% Strongly disagree: 3.0%

Society benefits from scientific information sharing and the latter should be independent of the scientific evaluation and promotion system



Strongly agree: 40.9% Somewhat agree: 34.2%

Neither agree nor disagree: 16.0%

Somewhat disagree: 5.5% Strongly disagree: 1.7%