



Animal research ethics: Taking the challenges seriously

Anna Olsson

Animal Research Tomorrow Webinar
13 November 2020

2010

- End of a long political and even longer technical process with extensive stakeholder engagement and lobbying
- Directive 2010/63/EU

nature Vol 464|15 April 2010

NEWS

Lab-animal battle reaches truce

Biomedical scientists say revised European directive on animal welfare averts feared disaster for research.

After more than a decade of pitched battles between research advocates and animal-rights campaigners, European Union (EU) legislators have finally agreed on a new legal framework to regulate the use of animals in research.

A closed-door meeting between representatives of the European Commission, the European Parliament and the European Council (respectively, the EU's executive and two legislative bodies) reached a compromise on a directive covering the protection of animals used for scientific purposes (86/609/EEC) on 7 April. The directive must still be ratified by the parliament and council, but this is likely to happen without further debate by July.

Previous drafts of the directive had seemed set to severely hamper European biomedical research by placing significant restrictions on



pointed out that this would be difficult for them to comply with, given that much of this information is proprietary intellectual property.

The battle continued through 2009 as the amended draft was discussed by the European Council, which comprises representatives of the EU's 27 member states, many of which considered it too liberal towards researchers. After a new parliament was elected last June, the animal-welfare lobby pounced on new members, convincing many to argue for further restrictions, says Julian Böcker, parliamentary assistant to directive rapporteur Elisabeth Jeggle. "I'd like to be able to convey just how hard we had to fight to maintain research-friendliness in the directive," says Böcker.

Endangered experiments

G. ROBERTSON/EVINE

2015

 STOP VIVISECTION



[Home](#) | [The initiative](#) | [Citizens' Committee](#) | [Supporters](#) | [Testimonials](#) | [BLOG!](#)

Home

What is animal experimentation (or vivisection)

Animal experimentation is a method of biomedical research based on the study of live animals and **therefore represents a fundamental methodological error**. The error consists in considering animals and **their tissues** as reliable models for **humans**. In reality every species is different from any other species (in anatomy, physiology, immunology, gene expression ... etc... even in its basic cellular structure) and each animal species can only be its own model. Substances that are extremely poisonous for humans are perfectly harmless for various laboratory **animal** species (see strychnine, hemlock, arsenic, mushroom "Amanita phalloides", etc.) and vice versa: the similarities between two species can be verified only "a posteriori", after the experiment has been repeated on the second species, namely the human. Never "a priori". This makes animal testing useless for humans and exposes us to serious risks with regard to our future well-being.

Learn more:

- ✓ [What is animal experimentation](#)
- ✓ [Links to Scientific Reports](#)
- ✓ [Links to Media Articles](#)
- ✓ [Quotes by Experts](#)
- ✓ [Quotes by Scientific Articles](#)
- ✓ [Why we say No to Dir. 2010/63/EU](#)
- ✓ [Interviews](#)
- ✓ [Regulation REACH](#)
- ✓ [Health Titanic](#)
- ✓ [Statistical data](#)

- One of the first Citizen's Initiative to receive enough support for submission to the European Commission



Stop Vivisection argued that:

- It is increasingly recognized that animal experimentation has no predictive value for humans
- Therefore, animal experimentation is a hazard for human health and an obstacle for development of new methods, and slows down scientific progress
- Need to act against the strong interests of profit from animal experimentation without respect for human health and the right to life, liberty and welfare, of all living beings.



2015

STOP VIVISECTION



[Home](#) | [The initiative](#) | [Citizens' Committee](#) | [Supporters](#) | [Testimonials](#) | [BLOG!](#)

Home

What is animal experimentation (or vivisection)

Animal experimentation is a method of biomedical research based on the study of live animals and **therefore represents a fundamental methodological error**. The error consists in considering animals and **their tissues** as reliable models for **humans**. In reality every species is different from any other species (in anatomy, physiology, immunology, gene expression ... etc... even in its basic cellular structure) and each animal species can only be its own model. Substances that are extremely poisonous for humans are perfectly harmless for various laboratory **animal** species (see strychnine, hemlock, arsenic, mushroom "Amanita phalloides", etc.) and vice versa: the similarities between two species can be verified only "a posteriori", after the experiment has been repeated on the second species, namely the human. Never "a priori". This makes animal testing useless for humans and exposes us to serious risks with regard to our future well-being.

ADVERTISING



[Read the coverage here](#)

Learn

- ✓ [What is](#)
- ✓ [Links to](#)
- ✓ [Links to](#)
- ✓ [Quote:](#)
- ✓ [Quote:](#)
- ✓ [Why w](#)
- ✓ [Intervi](#)
- ✓ [Regula](#)
- ✓ [Health](#)
- ✓ [Statist](#)

MEPs unconvinced by European Citizens' Initiative on vivisection

[Home](#) | [Science & Policymaking](#) | [News](#)

By [Aline Robert](#) | [EurActiv.fr](#) | Translated By [Samuel White](#)

📅 15/05/2015





However, >1 million EU citizens were / are convinced that

Animal experimentation is wrong because:

- It is not useful
- It harms the animals

CORRIERE DELLA SERA

Lunedì 21 Ottobre 2013 Corriere della Sera

VIVISEZIONE

Le inutili sofferenze degli animali

di JEREMY RIFKIN

Avverte i grandi cambiamenti sociali volano al di sotto degli schermi radar. È ciò che sta avvenendo in questo momento in tutta l'Unione Europea. Un movimento di base dei cittadini per fermare la pratica insensata di sottoporre milioni di animali a sofferenze, dolore e alla morte nella sperimentazione di sostanze chimiche tossiche che influiscono sulla salute umana sta riprendendo slancio in tutti i Paesi europei.

La campagna «Stop Vivisection» (www.stopvivisection.eu) si basa sull'articolo 11 del Trattato europeo, che sancisce il diritto di introdurre iniziative dei cittadini europei (Ice) e mobilitare un ampio sostegno popolare. Nell'ambito della procedura, se un milione di cittadini europei di almeno un quarto degli Stati membri la firmano, un'iniziativa dei cittadini può essere inviata automaticamente alla Commissione europea sotto forma di proposta di legge, dando così ai cittadini lo stesso diritto formale del Parlamento europeo e del Consiglio europeo di proporre norme.

L'iniziativa «Stop Vivisection» ha già raccolto più di 700.000 firme da tutta Europa e manca poco per raggiungere l'obiettivo di oltre 1 milione di firme.

Per anni, governi, aziende e ricercatori hanno sostenuto che gli esperimenti sugli animali per valutare il rischio delle sostanze chimiche per la salute umana sono fondamentali per garantire il benessere della nostra specie. Ora, invece, nuove scoperte nel campo della genomica, della bioinformatica, dell'epigenetica e della tossicologia computazionale stanno fornendo altri strumenti di ricerca per studiare le conseguenze delle sostanze chimiche tossiche sulla salute umana, che sono di gran lunga più precisi nella valutazione del rischio di queste sostanze per gli esseri umani.

Le associazioni antivivisezioniste e le organizzazioni per i diritti degli animali hanno sostenuto questo concetto per molti, molti anni, solo per essere disprezzate da organismi scientifici, associazioni mediche e dalle lobby industriali che le accusano di essere «contro il progresso» e di tenere più agli animali che alle persone. Ora è il mondo della scienza — fatto alquanto interessante — ad essere giunto alle stesse conclusioni.

Un certo numero di anni fa, il Consiglio nazionale delle ricerche della National academy of sciences, il principale organismo scientifico negli Stati Uniti, ha condotto un ampio studio per capire se e quanto sia ancora utile sottoporre milioni di animali a test di tossicità. Secondo i risultati della ricerca «i test attuali forniscono poche informazioni sulle modalità e sui meccanismi d'azione che sono fondamentali per la comprensione delle differenze inter-specie della tossicità e poche o nessuna informazione per valutare la variabilità e la sensibilità sugli esseri umani». In altre parole, milioni di animali ogni anno vengono sottoposti a sofferenze insensate e messi a morte nonostante il fatto che i test forniscono pochissime informazioni per la valutazione del rischio di queste sostanze chimiche per gli esseri umani. I test di tossicità sugli animali sono semplicemente scienza di infima categoria.

Il resoconto dell'Accademia nazionale delle scienze afferma che, per la prima volta, le nuove tecnologie d'avanguardia offrono la possibilità di ottenere dati più precisi sull'esposizione al rischio chimico. Infatti, gli autori del rapporto affermano «nel corso del tempo la necessità di condurre una sperimentazione animale dovrebbe essere notevolmente ridotta, e forse anche eliminata». Buone notizie per le creature che vivono insieme a noi.

Le nuove metodologie di analisi della tossicità

risparmieranno la vita di milioni di animali e allo stesso tempo manterranno la promessa di salvare la vita di milioni di esseri umani. Procedure di sperimentazione più rapide e più economiche e dati più precisi accellereranno la valutazione dei rischi dei prodotti chimici e forniranno gli strumenti per la creazione di nuovi farmaci e di altri interventi per garantire la nostra salute. In breve, questa nuova prospettiva porterà vantaggi sia per le creature che vivono con noi che per gli esseri umani.

Le persone possono essere in gran parte ignare del fatto che l'articolo 13 del Trattato sul funzionamento dell'Unione Europea riconosce che «poiché gli animali sono esseri senzienti», la formulazione e l'attuazione delle politiche comunitarie devono «tenere conto delle esigenze in materia di benessere degli animali, nel rispetto delle disposizioni legislative o amministrative e delle consuetudini degli Stati membri riguardanti in particolare i riti religiosi, le tradizioni culturali e il patrimonio regionale».

Con i nuovi modelli di ricerca e sperimentazione, non vi è più alcuna necessità di sottoporre milioni e milioni di animali alla sperimentazione disumana nei laboratori di ricerca. È giunto il momento di eliminare rapidamente le ricerche con vivisezione nei laboratori di tutta l'Unione Europea.

L'iniziativa Stop Vivisection dei Cittadini porta l'Europa e il mondo in una nuova era in cui estendiamo la nostra sensibilità empatica per le creature simili a noi, riconoscendo il loro diritto innato di esistere e di crescere insieme alla nostra specie qui sulla Terra.

Consigliere per l'Unione Europea
Presidente della Foundation
on Economic Trends a Washington

OPINIONE ESPRESSA



How well are we doing in ensuring that animal experiments are as useful as possible and causes as little harm as possible?



Are experiments on animals useful?

OPEN ACCESS Freely available online

PLOS MEDICINE

Research in Translation

Can Animal Models of Disease Reliably Inform Human Studies?

H. Bart van der Worp^{1*}, David W. Howells², Emily S. Sena^{2,3}, Michelle J. Porritt², Sarah Rewell², Victoria O'Collins², Malcolm R. Macleod³

¹Department of Neurology, Rudolf Magnus Institute of Neuroscience, University Medical Centre Utrecht, Utrecht, The Netherlands, ²National Stroke Research Institute & University of Melbourne Department of Medicine, Austin Health, Melbourne, Australia, ³Department of Clinical Neurosciences, University of Edinburgh, Edinburgh, United Kingdom

The screenshot shows a CBC News article page. At the top, there's a navigation bar with categories like News, Sports, Music, Radio, TV, My Region, More, Watch, Listen, and a search bar. Below that, the article title is 'Flaws in medical experiments on animals 'a waste'' with a sub-headline 'High failure rate in animal studies exposes people in trials to unsafe drugs'. The article text discusses the high failure rate of drugs tested in animals and the ethical concerns. There are social media sharing buttons for Facebook (104), Twitter (21), and Email. An 'External Links' box contains a link to a systematic review of guidelines for animal experiments. A photo of a woman holding a small white mouse is included. The article is dated July 23, 2013.



Evaluation of Excess Significance Bias in Animal Studies of Neurological Diseases

Konstantinos K. Tsilidis^{1,3}, Orestis A. Panagiotou^{1,3}, Emily S. Sena^{2,3}, Eleni Aretouli^{4,5}, Evangelos Evangelou¹, David W. Howells³, Rustam Al-Shahi Salman², Malcolm R. Macleod², John P. A. Ioannidis^{6*}

1 Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina, Greece, **2** Department of Clinical Neurosciences, University of Edinburgh, Edinburgh, United Kingdom, **3** The Florey Institute of Neuroscience and Mental Health, University of Melbourne, Heidelberg, Victoria, Australia, **4** Department of Methods and Experimental Psychology, University of Deusto, Bilbao, Spain, **5** Laboratory of Cognitive Neuroscience, School of Psychology, Aristotle University of Thessaloniki, Thessaloniki, Greece, **6** Stanford Prevention Research Center, Department of Medicine, and Department of Health Research and Policy, Stanford University School of Medicine, and Department of Statistics, Stanford University School of Humanities and Sciences, Stanford, California, United States of America

Abstract

Animal studies generate valuable hypotheses that lead to the conduct of preventive or therapeutic clinical trials. We assessed whether there is evidence for excess statistical significance in results of animal studies on neurological disorders, suggesting biases. We used data from meta-analyses of interventions deposited in Collaborative Approach to Meta-Analysis and Review of Animal Data in Experimental Studies (CAMARADES). The number of observed studies with statistically significant results (O) was compared with the expected number (E), based on the statistical power of each study under different assumptions for the plausible effect size. We assessed 4,445 datasets synthesized in 160 meta-analyses on Alzheimer disease ($n=2$), experimental autoimmune encephalomyelitis ($n=34$), focal ischemia ($n=16$), intracerebral hemorrhage ($n=61$), Parkinson disease ($n=45$), and spinal cord injury ($n=2$). 112 meta-analyses (70%) found nominally ($p \leq 0.05$) statistically significant summary fixed effects. Assuming the effect size in the most precise study to be a plausible effect, 919 out of 4,445 nominally significant results were expected versus 1,719 observed ($p < 10^{-9}$). Excess significance was present across all neurological disorders, in all subgroups defined by methodological characteristics, and also according to alternative plausible effects. Asymmetry tests also showed evidence of small-study effects in 74 (46%) meta-analyses. Significantly effective interventions with more than 500 animals, and no hints of bias were seen in eight (5%) meta-analyses. Overall, there are too many animal studies with statistically significant results in the literature of neurological disorders. This observation suggests strong biases, with selective analysis and outcome reporting biases being plausible explanations, and provides novel evidence on how these biases might influence the whole research domain of neurological animal literature.

ANALYSIS



Power failure: why small sample size undermines the reliability of neuroscience

Katherine S. Button^{1,2}, John P. A. Ioannidis³, Claire Mokrysz¹, Brian A. Nosek⁴, Jonathan Flint⁵, Emma S. J. Robinson⁶ and Marcus R. Munafò¹

Abstract | A study with low statistical power has a reduced chance of detecting a true effect, but it is less well appreciated that low power also reduces the likelihood that a statistically significant result reflects a true effect. Here, we show that the average statistical power of studies in the neurosciences is very low. The consequences of this include overestimates of effect size and low reproducibility of results. There are also ethical dimensions to this problem, as unreliable research is inefficient and wasteful. Improving reproducibility in neuroscience is a key priority and requires attention to well-established but often ignored methodological principles.

INSTITUTO
DE INVESTIGAÇÃO
E INOVAÇÃO
EM SAÚDE



Collaborative Approach to Meta Analysis and

•C•A•M•A•R•A•D•E•S•

Review of Animal Data from Experimental Studies

CAMARADES

OPEN ACCESS Freely available online

PLOS MEDICINE

Research in Translation

Can Animal Models of Disease Reliably Inform Human Studies?

H. Bart van der Worp^{1*}, David W. Howells², Emily S. Sena^{2,3}, Michelle J. Porritt², Sarah Rewell², Victoria O'Collins², Malcolm R. Macleod³

¹ Department of Neurology, Rudolf Magnus Institute of Neuroscience, University Medical Centre Utrecht, Utrecht, The Netherlands, ² National Stroke Research Institute & University of Melbourne Department of Medicine, Austin Health, Melbourne, Australia, ³ Department of Clinical Neurosciences, University of Edinburgh, Edinburgh, United Kingdom

INSTITUTO
DE INVESTIGAÇÃO
E INOVAÇÃO
EM SAÚDE
UNIVERSIDADE
DO PORTO



Critical translational aspects

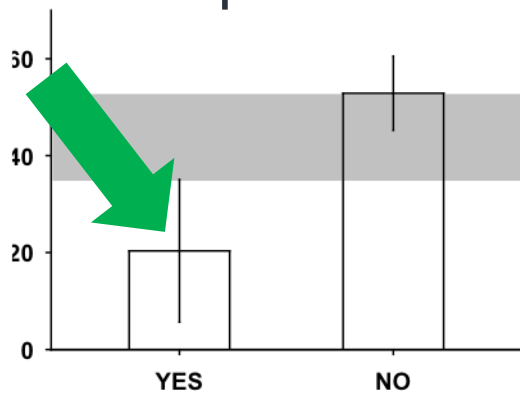
- Of human stroke patients, up to 75% are hypertense and up to 68% hyperglycaemic
 - About 10% of animal studies of focal ischaemia used hypertense and less than 1% hyperglycaemic animals
- A human stroke patient typically gets under treatment several hours, even days, after stroke
 - The median time between ischaemia onset and treatment in animal studies is 10 minutes

From van der Worp et al PLoSMedicine 7:3, March 2010

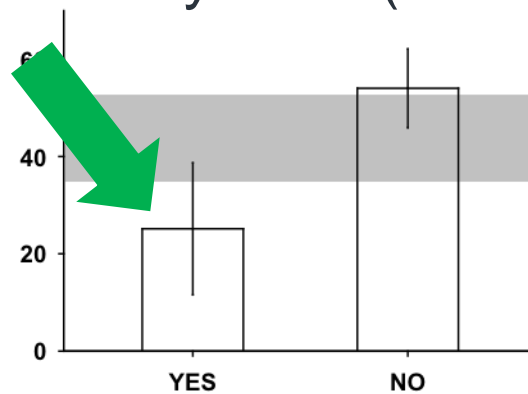
Critical aspects of good experimental practice

- NXY-059 (Astra Zeneca)
 - 11 publications, 29 experiments, 408 animals
 - Improved outcome by 44% (35-53%)

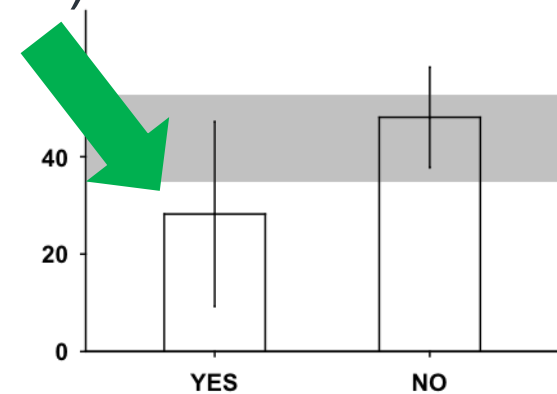
% improvement →



Randomisation



Blinded conduct of experiment



Blinded assessment of outcome

Macleod et al, 2008



Most animals used in research do not contribute to a published study

- 60% of approved animal protocols led to a publication within 7 years
- These publications correspond to 26% of the approved animal numbers

Open access

Original research

BMJ Open Science

Publication rate in preclinical research: a plea for preregistration

Mira van der Naald ^{1,2} Steven Wenker,¹ Pieter A Doevendans,^{1,3} Kimberley E Wever ⁴, Steven A J Chamuleau^{1,2}

To cite: van der Naald M, Wenker S, Doevendans PA, et al. Publication rate in preclinical research: a plea for preregistration. *BMJ Open Science* 2020;4:e100051. doi:10.1136/bmjos-2019-100051

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjos-2019-100051>).

Received 04 November 2019
Revised 15 February 2020
Accepted 27 April 2020

ABSTRACT

Objectives The ultimate goal of biomedical research is the development of new treatment options for patients. Animal models are used if questions cannot be addressed otherwise. Currently, it is widely believed that a large fraction of performed studies are never published, but there are no data that directly address this question.

Methods We have tracked a selection of animal study protocols approved in the University Medical Center Utrecht in the Netherlands, to assess whether these have led to a publication with a follow-up period of 7 years.

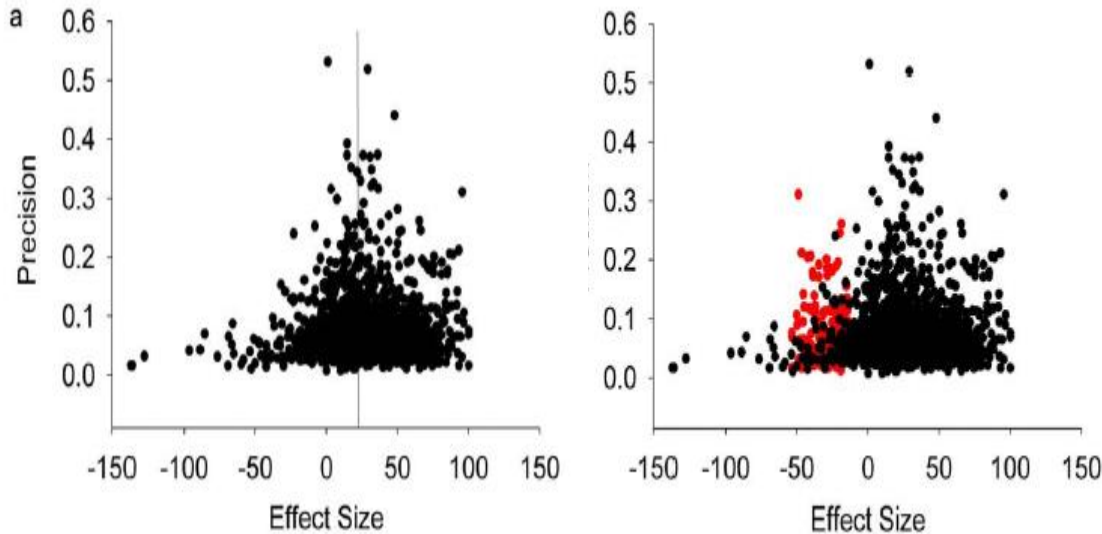
Results We found that 60% of all animal study protocols led to at least one publication (full text or abstract). A total of 5590 animals were used in these studies, of which 26% was reported in the resulting publications.

Conclusions The data presented here underline the need for preclinical preregistration, in view of the risk of reporting and publication bias in preclinical research. *Me*

Strengths and limitations of this study

- This study directly traces animal study protocols to potential publications and is the first study to assess the number of animals used and the number of animals published.
- We had full access to all documents submitted to the animal experiment committee of the University Medical Center Utrecht from the selected protocols.
- There is a sufficient follow-up period for researchers to publish their animal study.
- Due to privacy reasons, we are not able to publish the exact search terms used.
- A delay has occurred between the start of this project and time of publishing, this is related to the political sensitivity of this subject.

Publication bias may account for about 1/3 of the efficacy reported in systematic reviews



OPEN ACCESS Freely available online

PLoS BIOLOGY

Publication Bias in Reports of Animal Stroke Studies Leads to Major Overstatement of Efficacy

Emily S. Sena^{1,2,3}, H. Bart van der Worp⁴, Philip M. W. Bath⁵, David W. Howells^{2,3}, Malcolm R. Macleod^{1,6*}

¹ Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, United Kingdom, ² National Stroke Research Institute, Austin Health, University of Melbourne, Melbourne, Victoria, Australia, ³ Department of Medicine, Austin Health, University of Melbourne, Melbourne, Victoria, Australia, ⁴ Department of Neurology, Rudolf Magnus Institute of Neuroscience, University Medical Center, Utrecht, The Netherlands, ⁵ Stroke Trials Unit, University of Nottingham, Nottingham, England, United Kingdom, ⁶ Department of Neurology, NHS Forth Valley, Stirling, Scotland, United Kingdom

Abstract

The consolidation of scientific knowledge proceeds through the interpretation and then distillation of data presented in research reports, first in review articles and then in textbooks and undergraduate courses, until truths become accepted as such both amongst “experts” and in the public understanding. Where data are collected but remain unpublished, they cannot contribute to this distillation of knowledge. If these unpublished data differ substantially from published work, conclusions may not reflect adequately the underlying biological effects being described. The existence and any impact of such “publication bias” in the laboratory sciences have not been described. Using the CAMARADES (Collaborative Approach to Meta-analysis and Review of Animal Data in Experimental Studies) database we identified 16 systematic reviews of interventions tested in animal studies of acute ischaemic stroke involving 525 unique publications. Only ten publications (2%) reported no significant effects on infarct volume and only six (1.2%) did not report at least one significant finding. Egger regression and trim-and-fill analysis suggested that publication bias was highly prevalent (present in the literature for 16 and ten interventions, respectively) in animal studies modelling stroke. Trim-and-fill analysis suggested that publication bias might account for around one-third of the efficacy reported in systematic reviews, with reported efficacy falling from 31.3% to 23.8% after adjustment for publication bias. We estimate that a further 214 experiments (in addition to the 1,359 identified through rigorous systematic review; non-publication rate 14%) have been conducted but not reported. It is probable that publication bias has an important impact in other animal disease models, and more broadly in the life sciences.



Looking at the evidence

Can we claim to do enough to maximize benefit if:

- Aspects that are critical for translation and for reliable results are systematically overlooked
- The majority of animals used cannot be found in the publications resulting from research



Looking at the evidence

Can we claim to do enough to maximize benefit if:

- Aspects that are critical for translation and for reliable results are systematically overlooked
- The majority of animals used cannot be found in the publications resulting from research

What about harm – are we minimizing that?

Are we minimizing harm - pain?



ATLA 88, 119-127, 2005

119

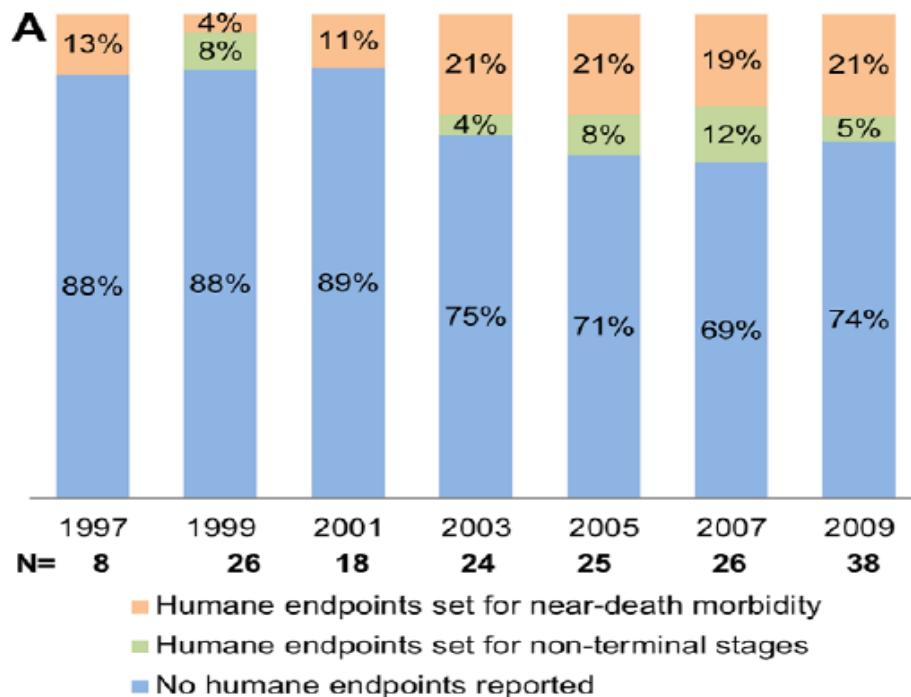
Anaesthesia and Post-operative Analgesia Following Experimental Surgery in Laboratory Rodents: Are We Making Progress?

Claire A. Richardson and Paul A. Flecknell

Comparative Biology Centre, University of Newcastle, Newcastle-upon-Tyne, UK

- Reported use of analgesia in potentially painful procedure in rodents
- An increase from 2.7% in 1990-92 to 19.8% in 2000-02

Are we minimizing harm – humane endpoints?



[available online](#)

Animal Welfare in Studies on Murine Tuberculosis: Assessing Progress over a 12-Year Period and the Need for Further Improvement

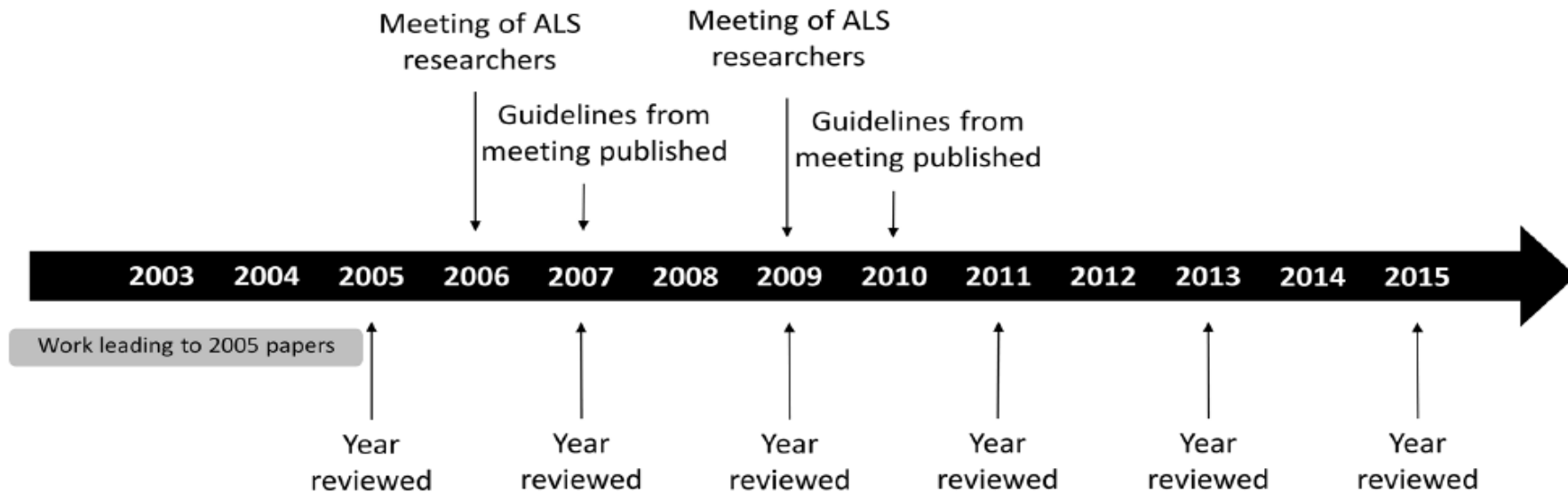
Nuno Henrique Franco^{1*}, Margarida Correia-Neves^{2,3}, I. Anna S. Olsson¹

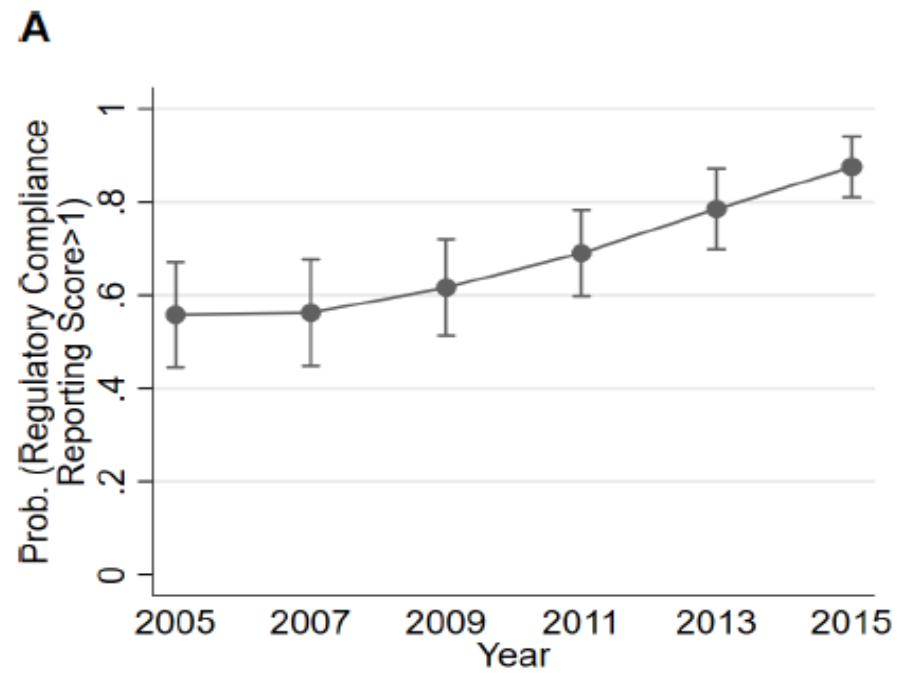
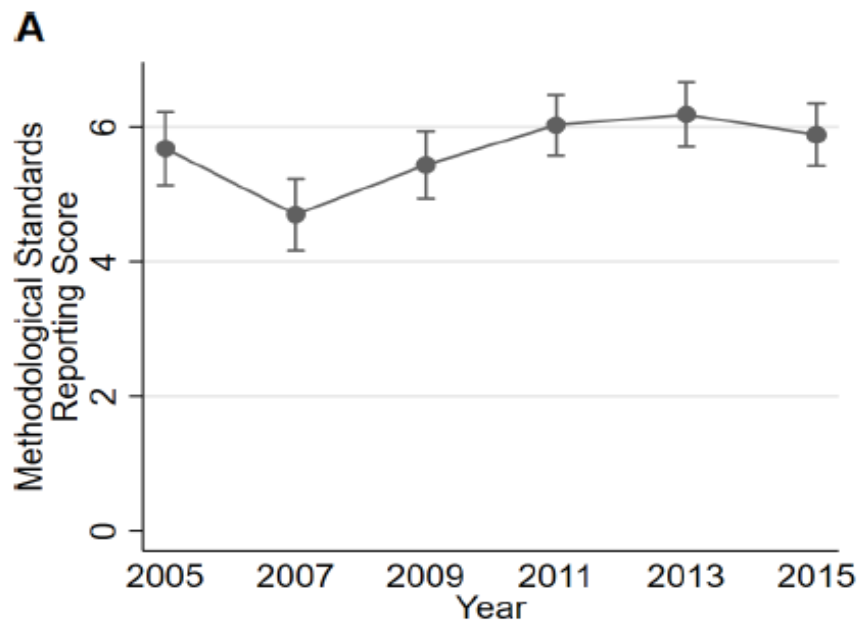
¹ IBMC - Institute for Molecular and Cell Biology (Laboratory Animal Science Group), University of Porto, Porto, Portugal, ² Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal, ³ ICVS/3B's - PT Government Associate Laboratory, Braga/Guimarães, Portugal



Methodological standards, quality of reporting and regulatory compliance in animal research on amyotrophic lateral sclerosis: a systematic review

Joana G Fernandes,^{1,2} Nuno H Franco,^{1,2} Andrew J Grierson,^{3,4} Jan Hultgren,⁵ Andrew J W Furley,^{4,6} I Anna S Olsson^{1,2}





Reported information	MSR score		'Proof-of-Concept' (n=461)		'Preclinical' (n=108)	
	Score item	Score weight	Absolute number	%	Absolute number	%
Relevant animal research variables						
Group size	<i>sampsize</i>	1.5	368	79.8	106	98.1
Environment: light, temperature, humidity (fully or partially reported)	<i>climate</i>	1	123	26.7	42	38.9
Cage size	<i>cagesize</i>	1	1	0.2	2	1.9
Mice per cage	<i>nmice</i>	1	26	5.6	15	13.9
Sex of the animals	<i>sex</i>	1.5	223	48.4	71	65.7
Number of transgene copies	<i>copies</i>	1.5	286	62.0	80	74.1
Genetic background	<i>genetic</i>	1.5	349	75.7	92	85.2
Measures to reduce 'noise' and bias in experiments						
Animals randomised to treatment groups	<i>random</i>	1	28	6.1	47	43.5
Observers blinded to treatment	<i>blinded</i>	1.5	94	20.4	52	48.1
Non-transgenic littermate controls used	<i>control</i>	1	150	32.5	39	36.1
Splitting littermates into groups	<i>sibsplit</i>	1	28	6.1	31	28.7
Reason for exclusion of animals is reported	<i>exclus</i>	1	2	0.4	6	5.6
	RCR score		'Proof-of-Concept' (n=461)		'Preclinical' (n=108)	
Self-reported compliance with laws and regulations	<i>comply</i>	1	98	21.3	28	25.9
Project approval reported	<i>protocol</i>	1	315	68.3	66	61.1
Refinement measures (eg, to aid, feed and hydrate)	<i>refine</i>	1	29	6.3	14	13

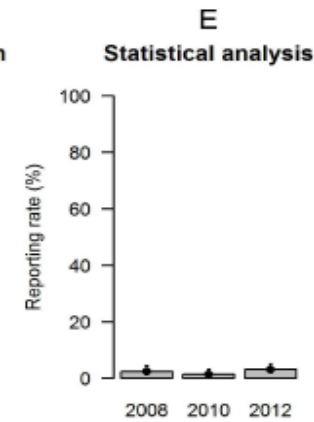
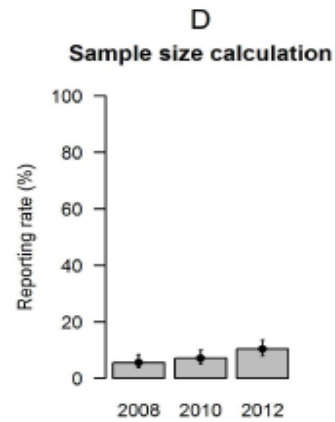
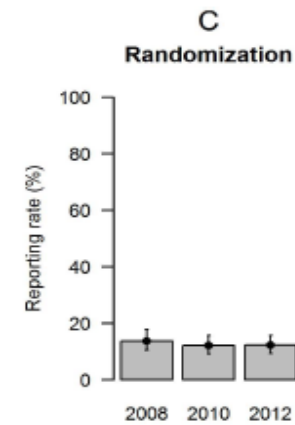
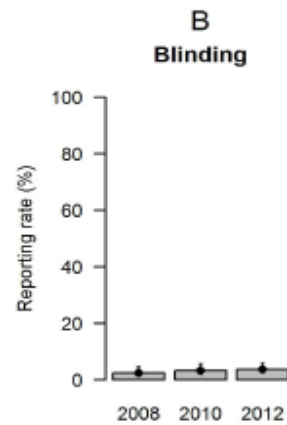
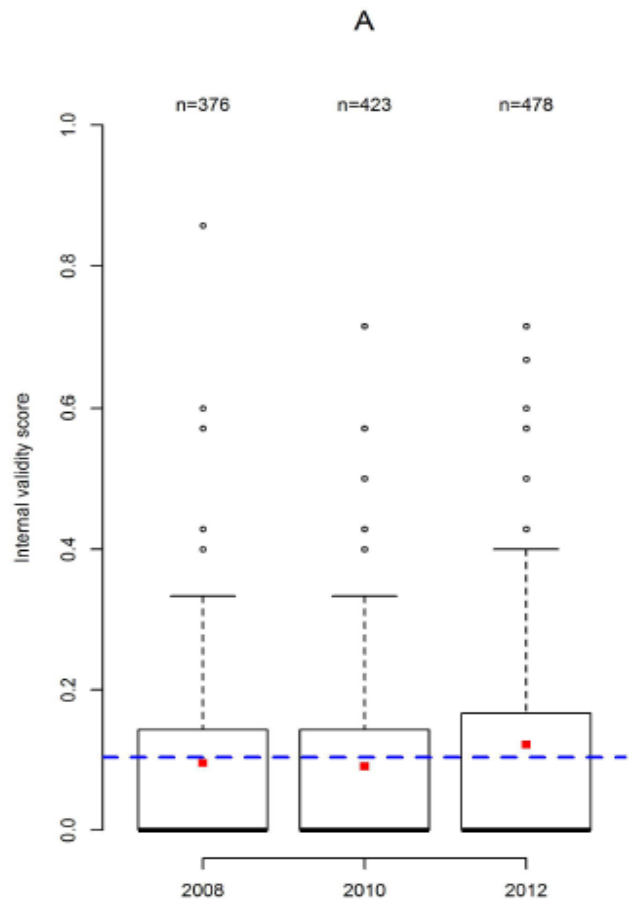
Reported information	MSR score		'Proof-of-Concept' (n=461)		'Preclinical' (n=108)	
	Score item	Score weight	Absolute number	%	Absolute number	%
Relevant animal research variables						
Group size	<i>sampsize</i>	1.5	368	79.8	106	98.1
Environment: light, temperature, humidity (fully or partially reported)	<i>climate</i>	1	123	26.7	42	38.9
Cage size	<i>cagesize</i>	1	1	0.2	2	1.9
Mice per cage	<i>nmice</i>	1	26	5.6	15	13.9
Sex of the animals	<i>sex</i>	1.5	223	48.4	71	65.7
Number of transgene copies	<i>copies</i>	1.5	286	62.0	80	74.1
Genetic background	<i>genetic</i>	1.5	349	75.7	92	85.2
Measures to reduce 'noise' and bias in experiments						
Animals randomised to treatment groups	<i>random</i>	1	28	6.1	47	43.5
Observers blinded to treatment	<i>blinded</i>	1.5	94	20.4	52	48.1
Non-transgenic littermate controls used	<i>control</i>	1	150	32.5	39	36.1
Splitting littermates into groups	<i>sibsplit</i>	1	28	6.1	31	28.7
Reason for exclusion of animals is reported	<i>exclus</i>	1	2	0.4	6	5.6
	RCR score		'Proof-of-Concept' (n=461)		'Preclinical' (n=108)	
Self-reported compliance with laws and regulations	<i>comply</i>	1	98	21.3	28	25.9
Project approval reported	<i>protocol</i>	1	315	68.3	66	61.1
Refinement measures (eg, to aid, feed and hydrate)	<i>refine</i>	1	29	6.3	14	13

Reported information	MSR score		'Proof-of-Concept' (n=461)		'Preclinical' (n=108)	
	Score item	Score weight	Absolute number	%	Absolute number	%
Relevant animal research variables						
Group size	<i>samplesize</i>	1.5	368	79.8	106	98.1
Environment: light, temperature, humidity (fully or partially reported)	<i>climate</i>	1	123	26.7	42	38.9
Cage size	<i>cagesize</i>	1	1	0.2	2	1.9
Mice per cage	<i>nmice</i>	1	26	5.6	15	13.9
Sex of the animals	<i>sex</i>	1.5	223	48.4	71	65.7
Number of transgene copies	<i>copies</i>	1.5	286	62.0	80	74.1
Genetic background	<i>genetic</i>	1.5	349	75.7	92	85.2
Measures to reduce 'noise' and bias in experiments						
Animals randomised to treatment groups	<i>random</i>	1	28	6.1	47	43.5
Observers blinded to treatment	<i>blinded</i>	1.5	94	20.4	52	48.1
Non-transgenic littermate controls used	<i>control</i>	1	150	32.5	39	36.1
Splitting littermates into groups	<i>sibsplit</i>	1	28	6.1	31	28.7
Reason for exclusion of animals is reported	<i>exclus</i>	1	2	0.4	6	5.6
	RCR score		'Proof-of-Concept' (n=461)	'Preclinical' (n=108)		
Self-reported compliance with laws and regulations	<i>comply</i>	1	98	21.3	28	25.9
Project approval reported	<i>protocol</i>	1	315	68.3	66	61.1
Refinement measures (eg, to aid, feed and hydrate)	<i>refine</i>	1	29	6.3	14	13



What is done to counter the problem?

- Guidelines for how to carry out research with animals
 - Discipline specific guidelines, PREPARE
- Review of animal experiments before they start
 - Ethics committees, IACUCs
- Guidelines for how to report research with animals
 - ARRIVE



Authorization of Animal Experiments Is Based on Confidence Rather than Evidence of Scientific Rigor

Lucile Vogt^{1*}, Thomas S. Reichlin^{1*}, Christina Nathues², Hanno Würbel^{1*}

1 Division of Animal Welfare, Veterinary Public Health Institute, Vetsuisse Faculty, University of Bern, Bern, Switzerland, **2** Division of VPH-Epidemiology, Veterinary Public Health Institute, Vetsuisse Faculty, University of Bern, Liebfeld, Switzerland



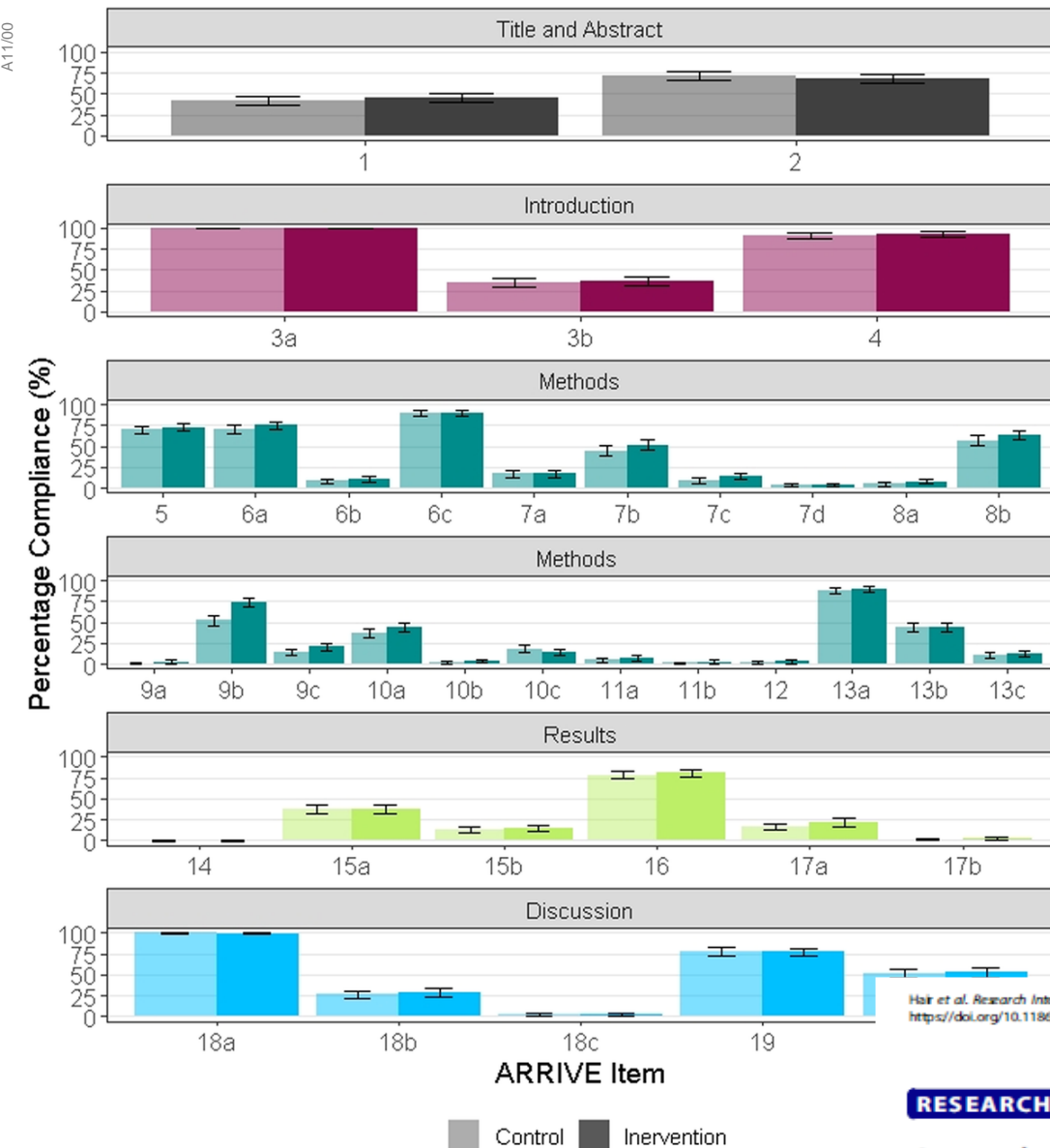
Despite widespread endorsement, the impact of ARRIVE has been limited



RESEARCH ARTICLE

ARRIVE has not ARRIVED: Support for the ARRIVE (Animal Research: Reporting of *in vivo* Experiments) guidelines does not improve the reporting quality of papers in animal welfare, analgesia or anesthesia

Vivian Leung[☉], Frédérik Rousseau-Blass[☉], Guy Beauchamp, Daniel S. J. Pang*



Hair et al. *Research Integrity and Peer Review*
<https://doi.org/10.1186/s41073-019-0069-3>




(2019) 4:12

Research Integrity and
Peer Review

RESEARCH

Open Access

A randomised controlled trial of an Intervention to Improve Compliance with the ARRIVE guidelines (IICARus)

Kaitlyn Hair , Malcolm R. Macleod , and Emily S. Sena , on behalf of the IICARus Collaboration





Why are we not doing better?

- This is a question of human attitudes and practice – social science is needed here!



RESEARCH ARTICLE

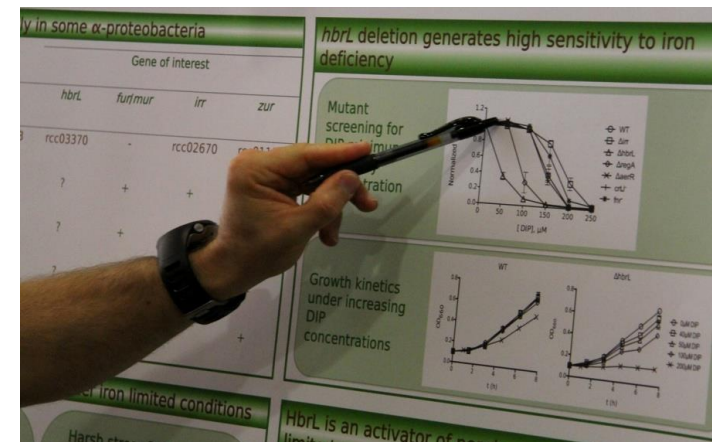
Developing a Collaborative Agenda for Humanities and Social Scientific Research on Laboratory Animal Science and Welfare

Gail F. Davies^{1*}, Beth J Greenhough², Pru Hobson-West³, Robert G. W. Kirk⁴, Ken Applebee⁵, Laura C. Bellingan⁶, Manuel Berdoy⁷, Henry Buller¹, Helen J. Cassaday⁸, Keith Davies⁹, Daniela Diefenbacher¹⁰, Tone Druglitrø¹¹, Maria Paula Escobar¹², Carrie Friese¹³, Kathrin Herrmann¹⁴, Amy Hinterberger¹⁵, Wendy J. Jarrett¹⁶, Kimberley Jayne¹⁷, Adam M. Johnson¹⁸, Elizabeth R. Johnson¹⁹, Timm Konold²⁰, Matthew C. Leach²¹, Sabina Leonelli²², David I. Lewis²³, Elliot J. Lilley²⁴, Emma R. Longridge²⁵, Carmen M. McLeod²⁶, Mara Miele²⁷, Nicole C. Nelson²⁸, Elisabeth H. Ormandy²⁹, Helen Pallett³⁰, Lonneke Poort³¹, Pandora Pound³², Edmund Ramsden³³, Emma Roe³⁴, Helen Scalway³⁵, Astrid Schrader³⁶, Chris J. Scotton³⁷, Cheryl L. Scudamore³⁸, Jane A. Smith³⁹, Lucy Whitfield⁴⁰, Sarah Wolfensohn⁴¹



Why are we not doing better?

- Practice in science is dependent on scientists' knowledge and attitude – those who perform the science and those who review it
- Incentives to do science right need to be as strong as prevalent incentives to publish in high-impact journals
- Changing minds take time





IS THERE A REPRODUCIBILITY CRISIS?



©nature

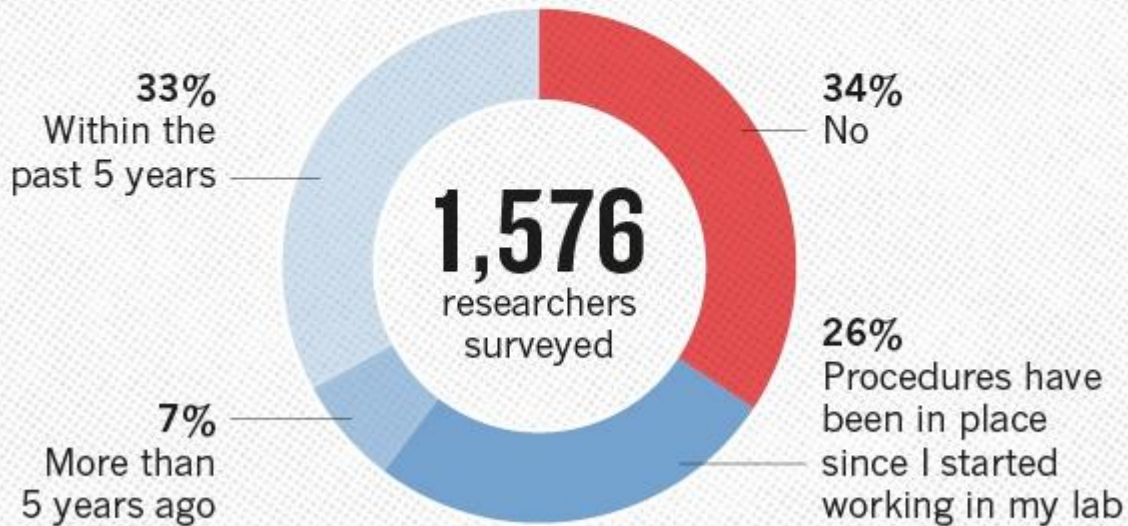
Nature May
2016

INSTITUTO
DE INVESTIGAÇÃO
E INOVAÇÃO
EM SAÚDE
UNIVERSIDADE
DO PORTO



HAVE YOU ESTABLISHED PROCEDURES FOR REPRODUCIBILITY?

Among the most popular strategies was having different lab members redo experiments.



©nature

Nature May
2016



3 important resources for the future

For better understanding

- Animal Research Nexus
 - Wellcome Trust research program for social science of animal research
 - <https://animalresearchnexus.org/>

For better practice

- Animal Study Registry
 - Pre-registration of animal studies similar to what is required for clinical trials
 - <https://www.animalstudyregistry.org>
- ARRIVE 2.0
 - Revised version for facilitated implementation
 - Focus on Essential 10
 - <https://arriveguidelines.org/>



Acknowledgements

- Nuno Franco, Margarida Correia-Neves, Joana Fernandes, Andrew Grierson and Andrew Furley for collaboration on methods assessment for preclinical research on TB and ALS
- Emily Sena and Malcolm Macleod for sharing material from methods assessment for preclinical stroke research
- Funding from FCT and European Commission



European legislation
Impact on the scientific use of animals

INSTITUTO
DE INVESTIGAÇÃO
E INOVAÇÃO
EM SAÚDE
UNIVERSIDADE
DO PORTO