



National Centre
for the Replacement
Refinement & Reduction
of Animals in Research

The ARRIVE guidelines: improving the reporting of *in vivo* research

Dr Vicky Robinson

The need for the ARRIVE guidelines

- Developed following an extensive review on the reporting of animals in research (Kilkenny et al., 2009).



- Survey of the quality of reporting of publically funded animal research in the UK and US.
- Co-funded by the MRC and the NIH Office of Laboratory Animal Welfare and commissioned by the NC3Rs.
- *In vivo* experiments involving rodents and non-human primates.
- 271 papers – most detailed survey of its kind.

Quality of published research

The survey identified key areas for improvement:

Experimental design

- Only 12% of publications report randomisation and 14% report blinding to reduce bias in animal selection and outcome measurements
- 38% of the studies amenable to a factorial design did not use one



Statistical analysis

- In 4% of the studies, it was unclear what statistical test had been used
- Only 70% of publications fully described statistical methods and presented the result with a measure of variability.



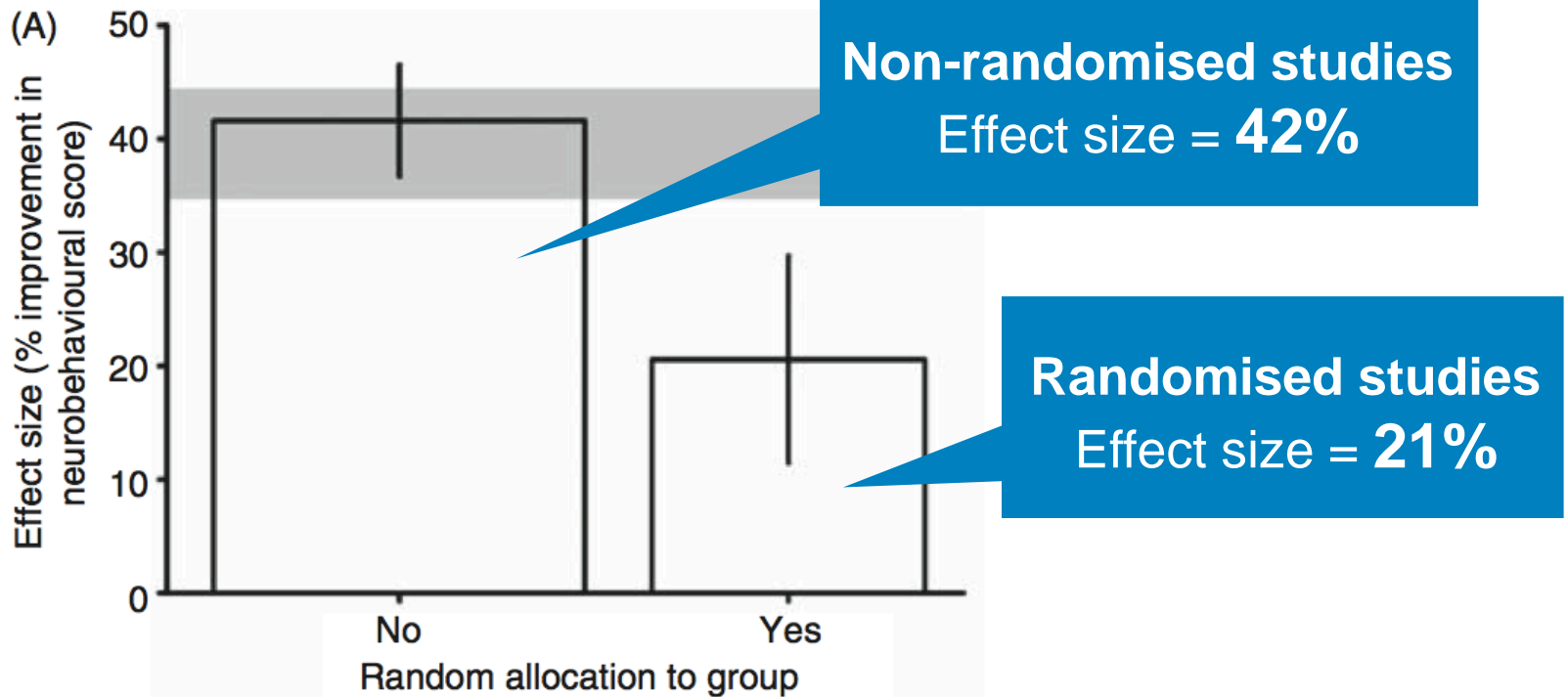
Reporting of studies

- Animal characteristics – missing in 25%
- Sample size – missing in 100%
- Only 59% stated the study hypothesis, number and characteristics of animals used



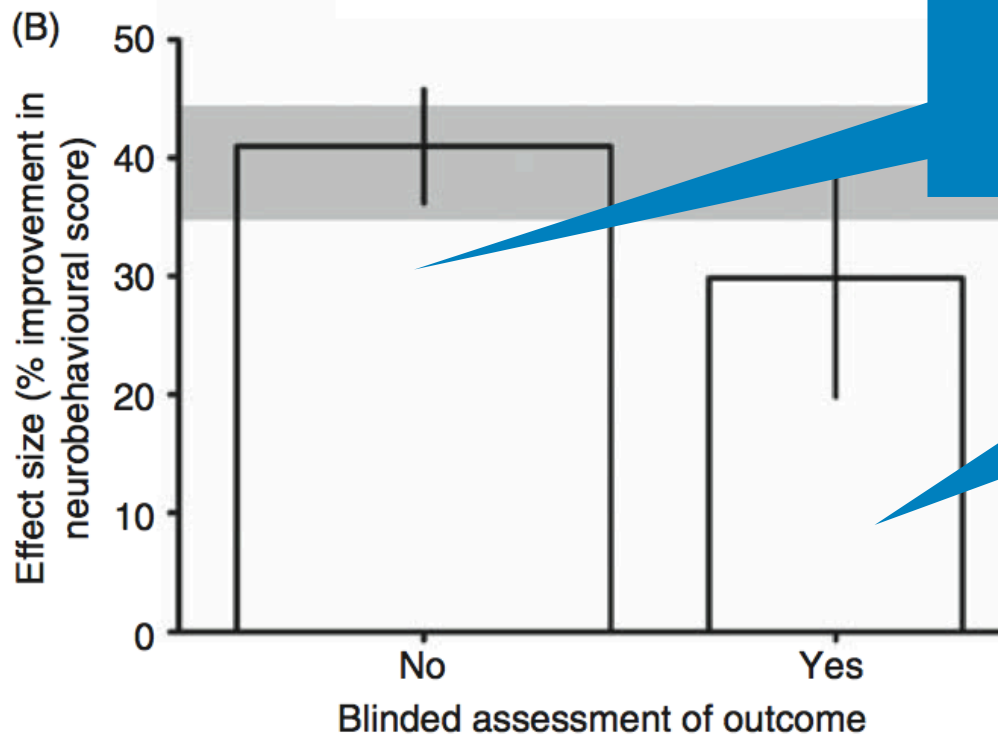
Quality of published research - Randomisation

- Animal models of multiple sclerosis
- Comparison of randomised and non-randomised studies



Quality of published research - Blinding

- Animal models of multiple sclerosis
- Comparison of blinded and non-blinded studies



Non-blinded studies
Effect size = **41%**

Blinded studies
Effect size = **30%**

Studies not blinded **overestimate** treatment efficacy

Supported by other reviews

Research Paper

Improving the translational hit of experimental treatments in multiple sclerosis

Hanna M Vesterinen, Emily S Sena, Charles French-Constant, Anna Williams, Siddharthan Chandran and Malcolm R Macleod

Multiple Sclerosis

Multiple Sclerosis
14(7) 1044-1055
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sagepub.com/journalsPermissions.nav
DOI: 10.1177/1352458510379612
msj.sagepub.com
SAGE

Assessment of statistical procedures used in papers in the Australian Veterinary Journal

IAN McCANCE
Editor of Publications, The Australian Physiological and Pharmacological Society,
PO Box 459, Mt Waverley, Victoria 3149

Multiple sclerosis

Veterinary research

Stroke

Pain

Journal of Cerebral Blood Flow
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www.jcbfm.com

Systematic review and metaanalysis of the efficacy of FK506 in experimental stroke

Malcolm R Macleod^{1,2}, Tori O'Collins¹, Laura L Horky¹, David W Howells^{1,3} and Geoffrey A Donnan^{1,3}

Pain 139 (2009) 243-247

Topical review

Animal models and the prediction of efficacy in clinical trials of analgesic drugs: A critical appraisal and call for uniform reporting standards

Andrew S.C. Rice^{a,*}, Dorothy Cimino-Brown^b, James C. Eisenach^c, Vesa K. Kontinen^d, Michael L. Lacroix-Fralish^e, Ian Machin^c,
(on behalf of the Preclinical Pain Consortium), Jeffrey S. Mogil^f, Thomas Stöhr^g

PAIN

www.elsevier.com/locate/pain

NC
3R^s

The guidelines include

Title

1. Accurate & concise description

Abstract

2. Background, objectives, methods, key findings and conclusions

Introduction

3. Background
4. Objectives

Methods

5. Ethical statement
6. Study design (blinding/randomisation)
7. Experimental procedures (How? When? Where? Why?)
8. Experimental animals (species, sex, weight)
9. Housing and husbandry
10. Sample size
11. Allocation experimental groups
12. Experimental outcomes
13. Statistical methods

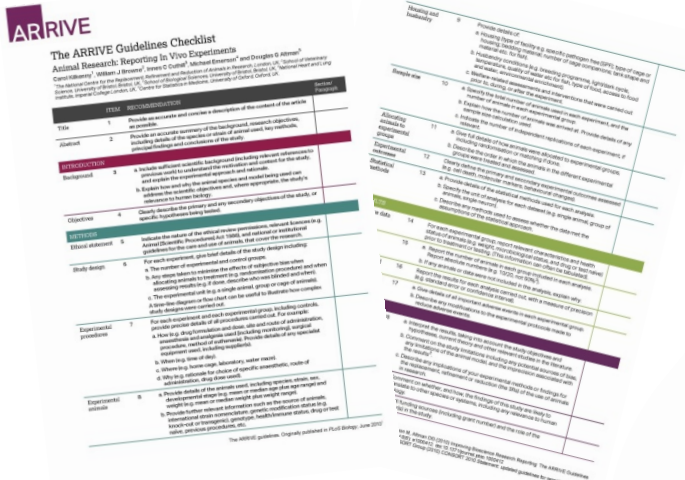
Results

14. Baseline Data
15. Numbers Analysed
16. Outcomes & estimation
17. Adverse events

Discussion

18. Interpretation & implications
19. Generalisability and translation
20. Funding

ARRIVE resources – www.nc3rs.org.uk/ARRIVE



Checklist



Translations

NC 3R^s National Centre for the Replacement, Refinement & Reduction of Animals in Research

The ARRIVE guidelines:
Animal Research: Reporting of In Vivo Experiments

Powering Better Science

ARRIVE guidelines?

ARRIVE guidelines were developed to improve the reporting of animal research. They are designed to be clear, concise and easy to use. They cover all aspects of animal research, from the design of the study to the reporting of the results.

Why should you use the ARRIVE?

- Improve the quality of your research
- Reduce the number of animals used
- Improve the reproducibility of your research
- Improve the transparency of your research
- Improve the credibility of your research

How can you use the ARRIVE?

- Use the ARRIVE guidelines to design your study
- Use the ARRIVE guidelines to report your results
- Use the ARRIVE guidelines to review your research
- Use the ARRIVE guidelines to teach your students

Conclusions & Further Information

The ARRIVE guidelines are designed to help you to report your research in a clear, concise and easy-to-use way. They are designed to be clear, concise and easy to use. They cover all aspects of animal research, from the design of the study to the reporting of the results.

www.nc3rs.org.uk/ARRIVE



National Centre for the Replacement, Refinement & Reduction of Animals in Research



The ARRIVE guidelines - Examples Animal Research: Reporting In Vivo Experiments

Carol Kilkenny¹, William J Brown², Innes C Cuthill³, Michael Emerson⁴ and Douglas G Altman⁵
¹The National Centre for the Replacement, Refinement and Reduction of Animals in Research, London, UK; ²School of Veterinary Science, University of Bristol, Bristol, UK; ³School of Biological Sciences, University of Bristol, Bristol, UK; ⁴National Heart and Lung Institute, Imperial College London, UK; ⁵Centre for Statistics in Medicine, University of Oxford, Oxford, UK

The ARRIVE guidelines are designed to improve the reporting of animal research. This document demonstrates how the ARRIVE guidelines can be used in practice to report animal research, by providing specific examples for each part of the guidelines. The examples given are from a wide range of research using a range of animal species. Each example has been chosen for meeting the criteria of the checklist mentioned and does not imply the entire manuscript complies with the ARRIVE guidelines.

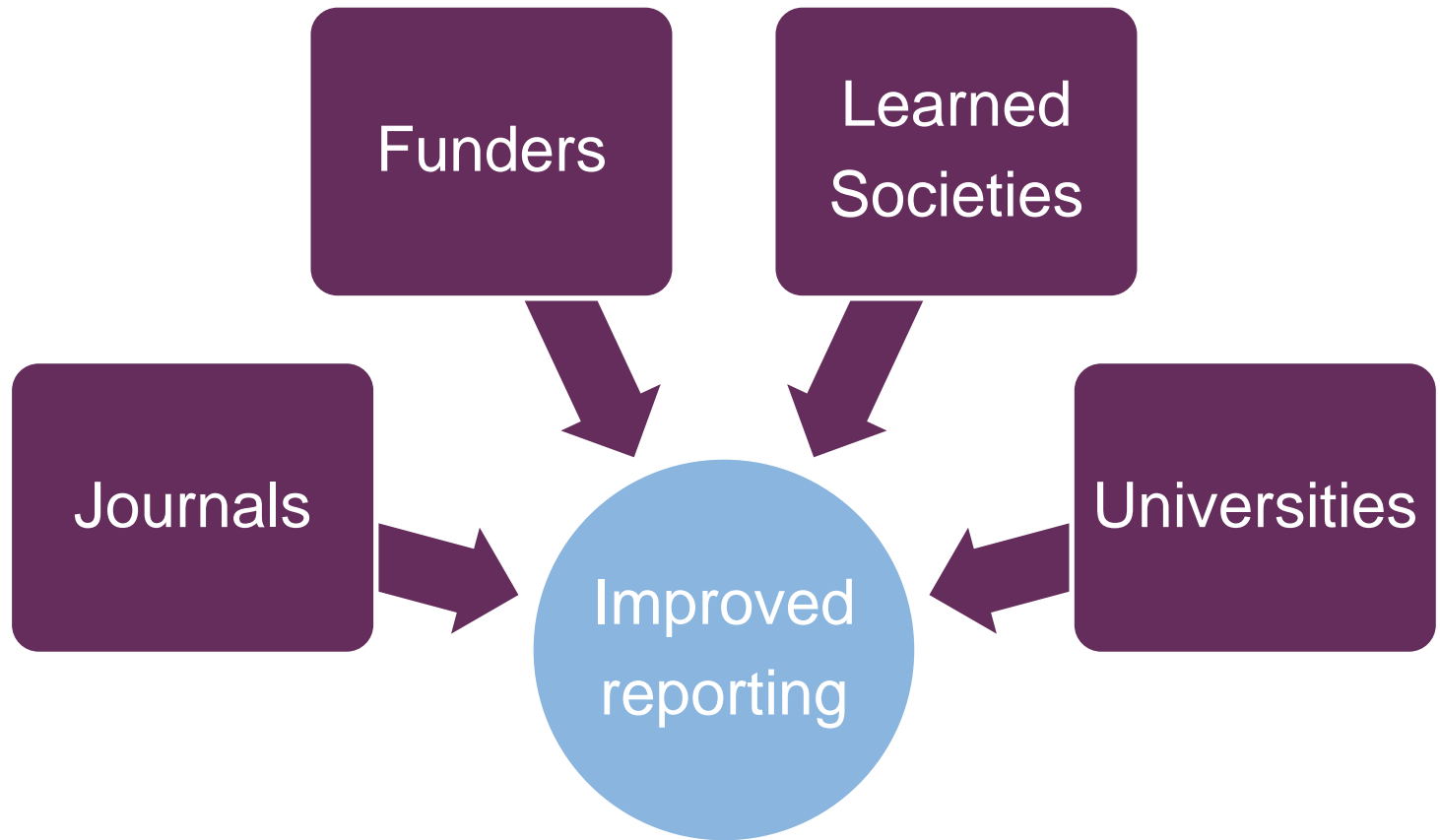
ITEM	RECOMMENDATION	EXAMPLE
TITLE	1 Provide an accurate and concise description of the content of the article as possible	Thoracic cage plasticity in prepubertal New Zealand white rabbits submitted to T1-T12 dorsal arthrodesis: computed tomography evaluation, echocardiographic assessment and cardio-pulmonary measurements (Cassese et al., 2013)
ABSTRACT	2 Provide an accurate summary of the background, research objectives, including details of the species or strain of animal used, key methods, principal findings and conclusions of the study	<p>BACKGROUND AND PURPOSE Asthma is an inflammatory disease that involves airway hyperresponsiveness and remodeling. Fluticasonide has been associated to anti-inflammatory and remodelling activities and may represent a potential therapeutic treatment of asthma. Our aim was to evaluate the effects of the salutaridin treatment in several aspects of experimental asthma model in mice.</p> <p>EXPERIMENTAL APPROACH Male BALB/c mice received ovalbumin (o) on days D and 14, and were challenged with aerosolized ovalbumin 1% on days 24, 28 and 32. Challenge-associated animals received vehicle (saline) and dimethyl sulfoxide (DMSO), salutaridin (20 mg/kg ip/mice) or dexamethasone (5 mg/kg ip) per mice daily beginning from 24h to 28th day. Control group received saline evaluation and nasal drug vehicle. On day 28 we determined the airway hyperresponsiveness, inflammation and remodeling as well as specific IgE antibody (RASTES) (i.e. IgE-EA). Eosinophils (Eo), Th1-a, Th1-g and GM-CSF content in lung homogenate was performed by Biosay assay, and 8-isoprostane and NF-κB activations were visualized in inflammatory cells by immunohistochemistry.</p>

Presentation and speaker notes

Examples



Strategy for adoption of the ARRIVE guidelines



Who uses the ARRIVE guidelines?

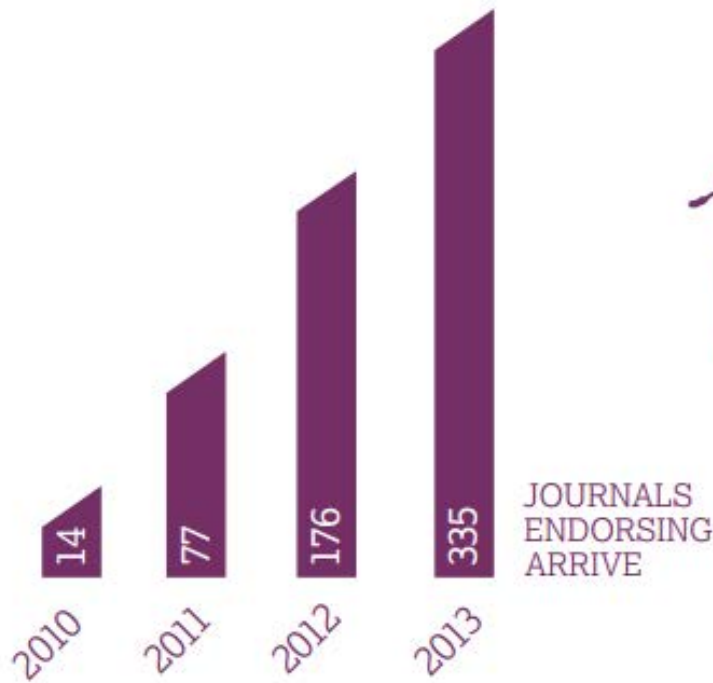


Over **7,000** copies of the ARRIVE Z card have been sent to **29** different countries.

Website visitors from **110** countries (www.nc3rs.org.uk/ARRIVE)

Journals endorsing ARRIVE

The ARRIVE guidelines are endorsed by **430** journals.



Funders endorsing ARRIVE

Open letter from UK funders to Universities to improve the design and reporting of animal research.

Signed by Chief Executives of UK bioscience research funders:

- Wellcome Trust
- BBSRC
- MRC

Since 2014...

22 May 2012

To: University Vice Chancellors, Principals and Heads of Divisions

As major funders of bioscience research in the UK we are committed to supporting the best science in terms of its conduct and impact. This is particularly the case with research involving the use of animals given the ethical implications, societal concerns and financial costs.

As part of this commitment we work closely with the NC3Rs, the Government-funded body which leads the delivery of new ways to replace, reduce and refine the use of animals. We have recently signed up to the NC3Rs guidelines – ARRIVE – which focus on improving the design and reporting of animal studies.

The NC3Rs has previously undertaken the largest survey to date of the quality of design, analysis and reporting of animal research, providing evidence that there is considerable scope for improvement. The ARRIVE guidelines are intended to help address this. Compliance with the guidelines is a condition of our grant funding.

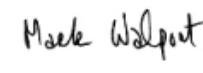
To ensure wide uptake and compliance with the ARRIVE guidelines, we are asking you to encourage scientists within your Institute to make use of the guidelines while designing experiments and reporting their research findings. The guidelines are endorsed by an increasing number of high impact journals and can be found at www.nc3rs.org.uk/ARRIVE.



Professor Sir John Savill
Chief Executive, MRC



Professor Douglas Kell
Chief Executive, BBSRC



Sir Mark Walport
Chief Executive, Wellcome Trust

Universities endorsing ARRIVE

Open letter from UK funders to Universities to improve the reporting of animal research.

- Institutional policies in animal research
- Public statement
- Licensee training courses
- Research training courses
- Internal communications



Societies endorsing ARRIVE

A growing number of learned societies are endorsing the ARRIVE guidelines and sharing with their members:



Further information

www.nc3rs.org.uk/ARRIVE

www.nc3rs.org.uk

@NC3Rs