ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA

Corso di Formazione per il personale abilitato in materia di IMPIEGO DEGLI ANIMALI A FINI SCIENTIFICI ED EDUCATIVI

Ozzano dell'Emilia, 30 gennaio 2020

Linee Guida

ARRIVE & PREPARE e piattaforme

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Dipartimento di Scienze Mediche e Chirurgiche – Università di Bologna

Agenzia Italiana del Farmaco
AIFA

DICHIARAZIONE PUBBLICA DI INTERESSI, IMPEGNO ALLA RISERVATEZZA E CONSENSO AL TRATTAMENTO DEI DATI PERSONALI DEI SOGGETTI CHE COLLABORANO ALLE ATTIVITA' DELL'AIFA

Fabrizio De Ponti

Professore Ordinario di Farmacologia presso Alma Mater Studiorum, Università di Bologna

Tabella 1. DICHIARAZIONE PUBBLICA DI INTERESSI [1]

Interessi nell'industria farmaceutica	NO	Attualmente	Precedenti 2 anni	Da oltre 2 a 5 anni precedenti	Oltre 5 anni precedenti (facoltativo)
INTERESSI DIRETTI:					
1. Impiego in una società	☒	☐	☐	☐	☐
2. Consulenza per una società	☒	☐	☐	☐	☐
3. Consulente strategico per una società	☒	☐	☐	☐	☐
4. Interessi finanziari	☒	☐	☐	☐	☐
5. Titolarità di un brevetto	☒	☐	☐	☐	☐
INTERESSI INDIRETTI:					
6. Sperimentatore principale	☒	☐	☐	☐	☐
7. Sperimentatore	☒	☐	☐	☐	☐
8. Sovvenzioni o altri fondi finanziari	☒	☐	☐	☐	☐

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ARRIVE

(Animal Research: Reporting of In Vivo Experiments)

The ARRIVE guidelines, originally published in PLOS Biology, were developed in consultation with the scientific community as part of an **NC3Rs initiative** to improve the standard of reporting of research using animals.

https://www.nc3rs.org.uk/arrive-guidelines

PREPARE

(Planning Research and Experimental Procedures on Animals: Recommendations for Excellence)

Norecopa is a member of *ecopa* (European Consensus-Platform for Alternatives), hence the name. Norecopa has produced the PREPARE guidelines for planning animal research and testing

ecopa was founded following an initiative at the *3rd World Congress on Alternatives and Animal Use* in Bologna in 1999, and supports National Consensus Platforms for the 3Rs.

https://norecopa.no/about-norecopa

Be PREPARED before you ARRIVE !

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Some of the areas which can be neglected ...

- poor literature searches
- lack of humane endpoints
- poor experimental design
- vague distribution of work and costs between the scientists and the animal facility
- insufficient evaluation of the facility's competence and infrastructure
- too little attention to transport and acclimation
- ignoring health risks for all involved
- lack of standard procedures for necropsy
- poor planning of waste disposal
- little discussion about the fate of the animals

Check for updates

Original Article

PREPARE: guidelines for planning animal research and testing

Adrian J Smith[1], R Eddie Clutton[2], Elliot Lilley[3], Kristine E Aa Hansen[4] and Trond Brattelid[5]

Laboratory Animals
2018, Vol. 52(2) 135–141

DOI: 10.1177/0023677217724823
journals.sagepub.com/home/lan
SAGE

Abstract

There is widespread concern about the quality, reproducibility and translatability of studies involving research animals. Although there are a number of reporting guidelines available, there is very little overarching guidance on how to *plan* animal experiments, despite the fact that this is the logical place to start ensuring quality. In this paper we present the PREPARE guidelines: Planning Research and Experimental Procedures on Animals: Recommendations for Excellence. PREPARE covers the three broad areas which determine the quality of the preparation for animal studies: formulation, dialogue between scientists and the animal facility, and quality control of the various components in the study. Some topics overlap and the PREPARE checklist should be adapted to suit specific needs, for example in field research. Advice on use of the checklist is available on the Norecopa website, with links to guidelines for animal research and testing, at https://norecopa.no/PREPARE.

Keywords

guidelines, planning, design, animal experiments, animal research

Date received: 5 April 2017; accepted: 27 June 2017

Introduction

The quality of animal-based studies is under increasing scrutiny, for good scientific and ethical reasons. Studies of papers reporting animal experiments have revealed alarming deficiencies in the information provided,[1,2] even after the production and journal endorsement of reporting guidelines.[3] There is also widespread concern about the lack of reproducibility and translatability of laboratory animal research.[4–7] This can, for example, contribute towards the failure of drugs when they enter human trials.[8] These issues come in addition to other concerns, not unique to animal research, about publication bias, which tends to favour the reporting of positive results and can lead to the acceptance of claims as fact.[9] This has understandably sparked a demand for reduced waste when planning experiments involving animals.[10–12] Reporting guidelines alone cannot solve the problem of wasteful experimentation, but thorough planning will increase the likelihood of success and is an important step in the implementation of the 3Rs of Russell & Burch (replacement, reduction, refinement).[13] The importance of attention to detail at all stages is, in our experience, often underestimated by scientists. Even small practical details can cause omissions or artefacts that can ruin experiments which in all other respects have been well-designed, and generate health risks for all involved. There is therefore, in our opinion, an urgent need for detailed but overarching guidelines for researchers on how to plan animal experiments which are safe and scientifically sound, address animal

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[3]Research Animals Department, Science Group, RSPCA, Southwater, Horsham, West Sussex, UK
[4]Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, Oslo, Norway
[5]Division for Research Management and External Funding, Western Norway University of Applied Sciences, Bergen, Norway

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Published in the April 2018 issue of Laboratory Animals

http://journals.sagepub.com/doi/full/10.1177/0023677217724823

https://norecopa.no/prepare/presentation

An example: i.v. injection of a radioactive isotope:

procedureswithcare.org.uk/intravenous-injection-in-the-mouse

norecopa.no/PREPARE

PREPARE Checklist | 1-Literature searches | 2-Legal issues |
3-Ethical issues, Harm-Benefit Assessment and humane endpoints | 4-Experimental design and statistical analysis |
5-Objectives and timescale, funding and division of labour | 6-Facility evaluation | 7-Education and training |
8-Health risks, waste disposal and decontamination | 9-Test substances and procedures | 10-Experimental animals
11-Quarantine and health monitoring | 12-Housing and husbandry | 13-Experimental procedures |
14-Humane killing, release, re-use or re-homing | 15-Necropsy | Comparison with ARRIVE

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PREPARE

Formulation of the study

1. Literature searches
2. Legal issues
3. Ethical issues, Harm-Benefit Assessment and humane endpoints
4. Experimental design and statistical analysis

Dialogue between scientists and the animal facility

5. Objectives and timescale, funding and division of labour
6. Facility evaluation
7. Education and training
8. Health risks, waste disposal and decontamination

Quality control of the components in the study

9. Test substances and procedures
10. Experimental animals
11. Quarantine and health monitoring
12. Housing and husbandry
13. Experimental procedures
14. Humane killing, release, re-use or re-homing
15. Necropsy

ARRIVE

1. Title
2. Abstract

Introduction

3. Background
4. Objectives

Methods

5. Ethical statement
6. Study design
7. Experimental procedures
8. Experimental animals
9. Housing and husbandry
10. Sample size
11. Allocating animals to experimental groups
12. Experimental outcomes
13. Statistical methods

Results

14. Baseline data
15. Numbers analysed
16. Outcomes and estimation
17. Adverse events

Discussion

18. Interpretation/scientific implications
19. Generalisability/translation
20. Funding

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PREPARE:

Planning **R**esearch and **E**xperimental **P**rocedures on **A**nimals: **R**ecommendations for **E**xcellence

PREPARE covers 15 topics:

Formulation of the study

1. Literature searches
2. Legal issues
3. Ethical issues, harm-benefit assessment and humane endpoints
4. Experimental design and statistical analysis

Dialogue between scientists and the animal facility

5. Objectives and timescale, funding and division of labour
6. Facility evaluation
7. Education and training
8. Health risks, waste disposal and decontamination

Methods

9. Test substances and procedures
10. Experimental animals
11. Quarantine and health monitoring
12. Housing and husbandry
13. Experimental procedures
14. Humane killing, release, reuse or rehoming
15. Necropsy

Items in pink are not highlighted in ARRIVE

Ancora linee guida?

NC 3Rs

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

The ARRIVE guidelines

Animal Research: Reporting of *In Vivo* Experiments

Traduzione Italiana

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Come siamo giunti ad ARRIVE & PREPARE?

… motivazione scientifica ed etica

(foto Antoine Mangiavacca / Klape)

Sperimentazione Animale: Stakeholders

	Progresso scientifico	Salute animali	Salute umana	Profitto
Cittadino	X	XXXX	XX	--
Sperimentatore	XXXX	XX	XX	XX
Azienda farmaceutica	XX	XX	XX	XXXX
Sistema Italia	XX	XX	XX	XX

COSTITUZIONE

DELLA REPUBBLICA ITALIANA

Art. 9 - La Repubblica promuove lo sviluppo della cultura e la **ricerca scientifica e tecnica**

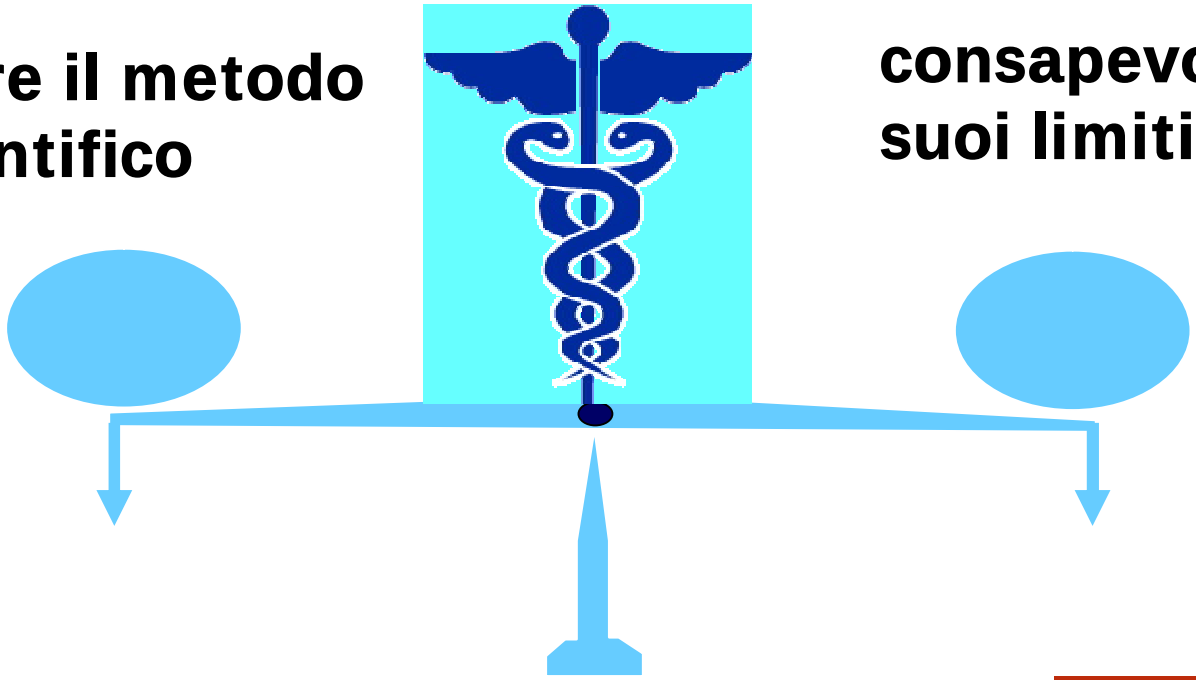
Art. 33 - **L'arte e la scienza sono libere e libero ne è l'insegnamento.**

...

Le istituzioni di alta cultura, **università** ed accademie, hanno il diritto di darsi **ordinamenti autonomi** nei limiti stabiliti dalle leggi dello Stato.

LA RICERCA OGGI

usare il metodo scientifico



consapevoli dei suoi limiti

Che cos’è una pubblicazione scientifica?

Una pubblicazione si può definire “scientifica” se soddisfa contemporaneamente tutti i quattro criteri sottoelencati:

1.i risultati presentati hanno caratteri di **originalità**;

2. i risultati sono presentati in una **forma atta alla verifica e/o al riuso** in attività di ricerca;

3. la lingua utilizzata e la distribuzione sono tali da rendere la pubblicazione **accessibile** alla maggior parte dei ricercatori potenzialmente interessati;

4. la sede editoriale (rivista, collana, monografia, sito *web*) assicura sistematicamente l’esistenza di una ***peer review* esterna**

Improved design and reporting for human clinical trials

Annals of Internal Medicine | ACADEMIA AND CLINIC

CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomized Trials

Kenneth F. Schulz, PhD, MBA; Douglas G. Altman, DSc; and David Moher, PhD for the CONSORT Group*

The CONSORT (Consolidated Standards of Reporting Trials) statement is used worldwide to improve the reporting of randomized, controlled trials. Schulz and colleagues describe the latest version, CONSORT 2010, which updates the reporting guideline based on new methodological evidence and accumulating experience.

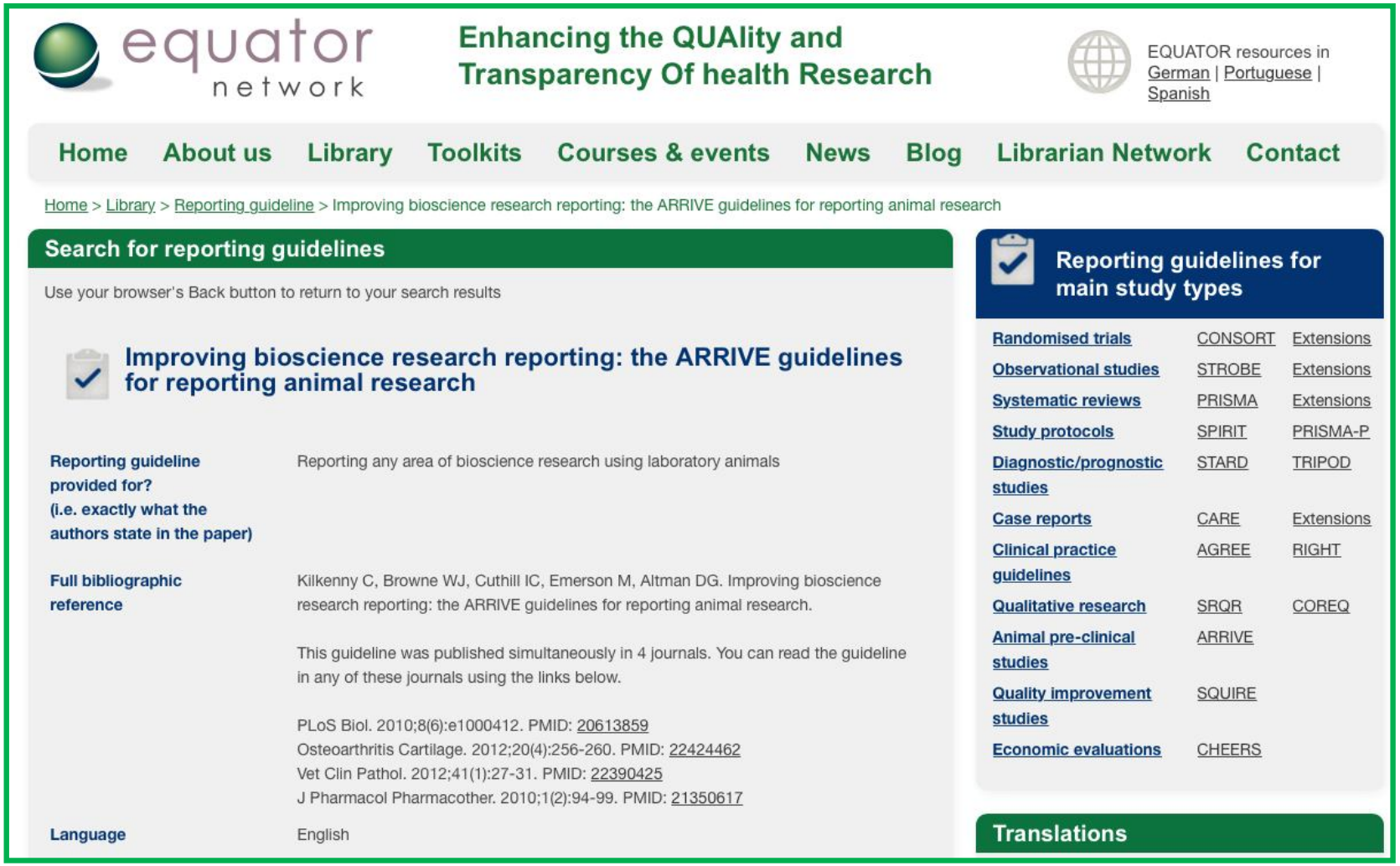
Ann Intern Med. 2010;152. www.annals.org

For author affiliations, see end of text.

* For the CONSORT Group contributors to CONSORT 2010, see the Appendix, available at www.annals.org.

This article was published at www.annals.org on 24 March 2010.

NON SOLO CONSORT ...



equator network

Enhancing the QUAlity and Transparency Of health Research

EQUATOR resources in German | Portuguese | Spanish

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Home > Library > Reporting guideline > Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research

Search for reporting guidelines

Use your browser's Back button to return to your search results

Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research

Reporting guideline provided for? (i.e. exactly what the authors state in the paper)	Reporting any area of bioscience research using laboratory animals
Full bibliographic reference	Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG. Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research. This guideline was published simultaneously in 4 journals. You can read the guideline in any of these journals using the links below. PLoS Biol. 2010;8(6):e1000412. PMID: 20613859 Osteoarthritis Cartilage. 2012;20(4):256-260. PMID: 22424462 Vet Clin Pathol. 2012;41(1):27-31. PMID: 22390425 J Pharmacol Pharmacother. 2010;1(2):94-99. PMID: 21350617
Language	English

Reporting guidelines for main study types

Randomised trials	CONSORT	Extensions
Observational studies	STROBE	Extensions
Systematic reviews	PRISMA	Extensions
Study protocols	SPIRIT	PRISMA-P
Diagnostic/prognostic studies	STARD	TRIPOD
Case reports	CARE	Extensions
Clinical practice guidelines	AGREE	RIGHT
Qualitative research	SRQR	COREQ
Animal pre-clinical studies	ARRIVE	
Quality improvement studies	SQUIRE	
Economic evaluations	CHEERS	

Translations

http://www.equator-network.org

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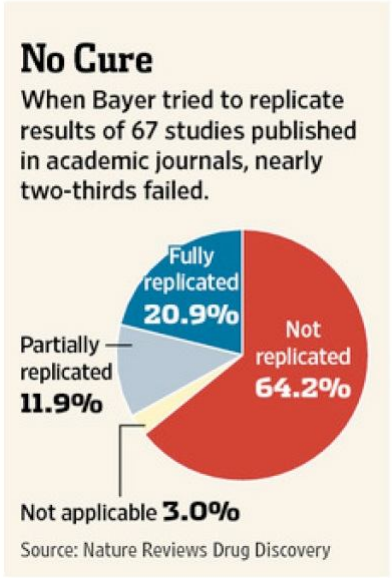
Quando i topi ci ingannano

Sena ES, van der Worp HB, Bath PM, Howells DW, Macleod MR. **Publication bias in reports of animal stroke studies leads to major overstatement of efficacy.** PLoS Biol. 2010;8(3)

Baker D, Lidster K, Sottomayor A, Amor S. **Reproducibility: Research-reporting standards fall short.** Nature 2012;492:4

Couzin-Frankel J. **When mice mislead.** Science 2013;342:922

Button KS, Ioannidis JP, Mokrysz C, Nosek BA, Flint J, Robinson ES, Munafò MR. **Power failure: why small sample size undermines the reliability of neuroscience.** Nat Rev Neurosci 2013;14:365



2011: WALL STREET JOURNAL

December 2, 2011
Scientists' Elusive Goal: Reproducing Study Results

http://www.omsj.org/corruption/scientists-elusive-goal-reproducing-study-results

2013: THE ECONOMIST

Unreliable research
Trouble at the lab
Oct 19th 2013

http://www.economist.com/news/briefing/21588057-scientists-think-science-self-correcting-alarming-degree-it-not-trouble

Università e sperimentazione animale:

uno sguardo storico

1) Gli anni pre-Direttiva 1986/609 (Regi Decreti)

2) La Direttiva 1986/609 e il D.Lgs. 116/1992

3) Applicazione della Direttiva 2010/63

4) Applicazione del D.Lgs. 26/2014

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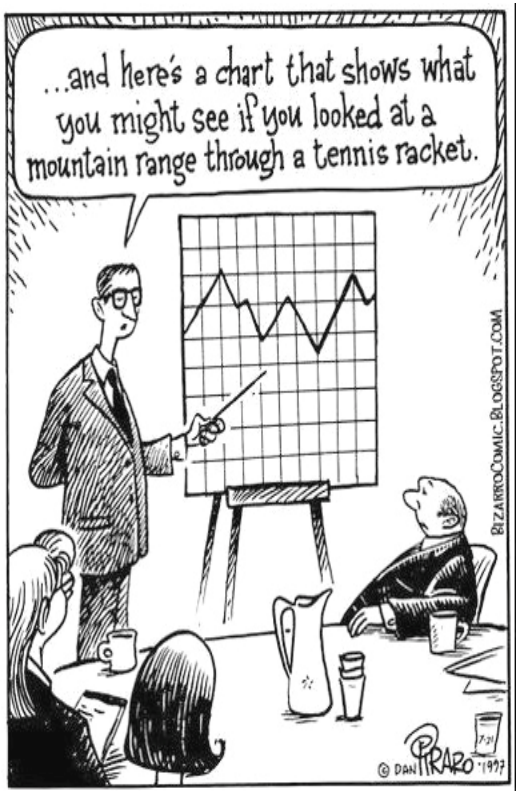
“Vediamo” attraverso uno specchio deformante



Un topo non è un “piccolo uomo”

"A mouse is not a mouse is not a mouse”

Ricercatori

necessitano di formazione specifica

Ambiente Accademico

premia i risultati positivi

incentiva la prolificità nel pubblicare

la scarsità di fondi non favorisce la numerosità del campione

Riviste Scientifiche

non applicano sistematicamente standard per garantire la qualità del report scientifico

Stampa divulgativa

tende ad esagerare i risultati

OPEN ACCESS Freely available online

PLoS BIOLOGY

Perspective

Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research

Carol Kilkenny[1]*, William J. Browne[2], Innes C. Cuthill[3], Michael Emerson[4], Douglas G. Altman[5]

1 The National Centre for the Replacement, Refinement and Reduction of Animals in Research, London, United Kingdom, **2** School of Veterinary Science, University of Bristol, Bristol, United Kingdom, **3** School of Biological Sciences, University of Bristol, Bristol, United Kingdom, **4** National Heart and Lung Institute, Imperial College London, United Kingdom, **5** Centre for Statistics in Medicine, University of Oxford, Oxford, United Kingdom

BJP British Journal of Pharmacology

DOI:10.1111/j.1476-5381.2010.00872.x
www.brjpharmacol.org

GUIDELINES

Animal research: Reporting *in vivo* experiments: The ARRIVE guidelines

Carol Kilkenny[1†], William Browne[2], Innes C Cuthill[3], Michael Emerson[4] and Douglas G Altman[5]

[1]*The National Centre for the Replacement, Refinement and Reduction of Animals in Research, London, UK,* [2]*Department of Clinical Veterinary Science, University of Bristol, UK,* [3]*School of Biological Sciences, University of Bristol, Bristol, UK,* [4]*National Heart and Lung Institute, Imperial College London, UK and* [5]*Centre for Statistics in Medicine, University of Oxford, Oxford, UK*

[†]Corresponding author. E-mail: carol.kilkenny@nc3rs.org.uk

J Physiol 588.14 (2010) pp 2519–2521

EDITORIAL

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

Journal of Cerebral Blood Flow & Metabolism (2011) 31, 991–993

www.jcbfm.com

Editorial

Animal research: reporting *in vivo* experiments—The ARRIVE Guidelines

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What are the ARRIVE guidelines?

The ARRIVE guidelines were developed as part of an NC3Rs initiative to improve the reporting of biomedical research using animals.

The ARRIVE guidelines consist of a checklist of 20 items, containing key information necessary to describe a study comprehensively and transparently.

The ARRIVE guidelines can be used to ensure reproducibility of animal research and avoid unnecessary animal use.

NC 3Rs

www.nc3rs.org.uk/ARRIVE

ARRIVE

ARRIVE - Traduzione Italiana

	ARTICOLO	RACCOMANDAZIONE
Titolo	1	Fornire una descrizione il più possibile accurata e concisa del contenuto dell'articolo.
Riassunto	2	Fornire un accurato riassunto delle conoscenze pregresse, degli obiettivi della ricerca, includendo i dettagli della specie o del ceppo degli animali usati, i metodi chiave, i principali risultati e le conclusioni dello studio.
INTRODUZIONE		
Conoscenze pregresse	3	a. Includere sufficienti conoscenze scientifiche pregresse (includendo le referenze più significative su lavori precedenti) per capire le motivazioni e il contesto dello studio, e spiegare l'approccio sperimentale e il razionale. b. Spiegare come e perché la specie animale e il modello che si utilizzeranno possono permettere di raggiungere gli obiettivi scientifici e, se pertinente, indicare la rilevanza dello studio per la biologia umana.
Obiettivi	4	Descrivere chiaramente gli obiettivi primari e secondari dello studio, o le ipotesi specifiche da verificare.
METODI		
Dichiarazione etica	5	Indicare la natura dei permessi etici, delle licenze (esempio: Animal [Scientific Procedures] Act 1986) e le linee guida nazionali o istituzionali relative alla cura e all'uso degli animali, che riguardano la ricerca.
Piano di studio	6	Per ogni esperimento, indicare sinteticamente i dettagli del piano di studio includendo: a. Il numero dei gruppi sperimentali e di controllo. b. Le procedure utilizzate per minimizzare gli effetti dell'influenza soggettiva quando si suddividono gli animali per il trattamento (esempio: randomizzazione) e quando si valutano i risultati (esempio: se svolto, descrivere chi era in cieco e quando). c. Le unità sperimentali (es. singolo animale, gruppi o gabbie di animali). Un diagramma con i tempi o un diagramma a flusso può essere utilizzato per illustrare come i piani di studi complessi vengono svolti.
Procedure sperimentali	7	Per ogni esperimento e ogni gruppo sperimentale, inclusi i controlli, fornire dettagli precisi di tutte le procedure svolte. Per esempio: a. Come (es. formulazione del farmaco e dose, sito e via di somministrazione, anestetico e analgesico utilizzati [incluso il monitoraggio], procedure chirurgiche, metodi di eutanasia). Fornire i dettagli di tutti gli strumenti specialistici usati, inclusi i fornitori. b. Quando (es. l'orario). c. Dove (es. gabbie, laboratorio, procedure comportamentali). d. Perchè (es.il razionale per la scelta di uno specifico anestetico, via di somministrazione, dose del farmaco utilizzata).
Animali sperimentali	8	a. Fornire i dettagli degli animali utilizzati, includendo la specie, ceppo, sesso, stadio di sviluppo (es. l'età media o media più l'intervallo di età) e il peso (es. media o mediana del peso più l'intervallo del peso). b. Fornire ulteriori informazioni di interesse come la provenienza degli animali, nomenclatura internazionale del ceppo, stato di modificazione genetica (es. knock-out o transgenico), genotipo, stato sanitario/immunologico, precedente esposizione a farmaci o test, procedure pregresse, etc.
Alloggio e allevamento	9	Fornire i dettagli di: a. Alloggio (tipo di stabulario, es. esente da specifici patogeni [SPF]; tipi di gabbie o alloggi; materiale della lettiera; numero di topi per gabbia; forma e materiale del contenitore per i pesci). b. Condizioni d'allevamento (es. programma di riproduzione, ciclo giorno/notte, temperatura, qualità dell'acqua etc. per i pesci, tipo di cibo, accesso al cibo e all'acqua, arricchimento ambientale). c. Valutazioni e interventi sullo stato di benessere che sono stati condotti prima, durante, o dopo l'esperimento.
Numerosità del campione	10	a.Specificare il numero complessivo degli animali impiegati in ogni esperimento, e il numero di animali presente in ogni gruppo sperimentale. b. Spiegare come si è ottenuto il numero di animali da utilizzare. Fornire dettagli sul calcolo utilizzato per selezionare il numero del campione. c. Indicare il numero di replicati indipendenti di ogni esperimento, se rilevante.
Distribuzione degli animali nei gruppi sperimentali	11	a. Fornire dettagli completi sulla distribuzione degli animali nei gruppi sperimentali, includendo la randomizzazione o la suddivisione rispetto a determinate caratteristiche, se vengono-effettuate. b. Descrivere l'ordine in cui gli animali sono stati trattati e valutati nei diversi gruppi sperimentali.
Risultati sperimentali	12	Definire chiaramente i risultati primari e secondari valutati (es. morte cellulare, marcatori molecolari, cambiamenti comportamentali).
Metodi statistici	13	a. Fornire i dettagli dei metodi statistici utilizzati per ogni analisi. b. Specificare l'unità di analisi per ogni gruppo di dati (es. singolo animale, gruppo di animali, singolo neurone). c. Descrivere i metodi usati per verificare se i dati sono coerenti con le assunzioni dell'approccio statistico.
RISULTATI		
Dati di riferimento	14	Per ogni gruppo sperimentale, riportare caratteristiche rilevanti e lo stato sanitario degli animali (es. peso, condizioni microbiologiche e esposizione precedente a farmaci o test) prima del trattamento o del test. (Queste informazioni possono essere schematizzate in una tabella).
Numeri analizzati	15	a. Riportare il numero di animali in ogni gruppo incluso in ogni analisi. Riportare il numero assoluto (es. 10/20, non 50%[4]). b. Se tutti gli animali oi dati non sono stati inclusi nell'analisi, spiegare la ragione.
Risultati e stime	16	Riportare i risultati per ogni analisi condotta, con una misura di precisione (es. errore standard o intervallo di confidenza).
Eventi avversi	17	a. Fornire i dettagli di tutti gli eventi avversi in ogni gruppo sperimentale. b. Descrivere le modifiche dei protocolli sperimentali finalizzate a ridurre gli eventi avversi.
DISCUSSIONE		
Interpretazione/ implicazioni scientifiche	18	a. Interpretare i risultati, tenendo in considerazione gli obiettivi del progetto e le ipotesi, le conoscenze attuali e gli studi di riferimento presenti in letteratura. b. Commentare le limitazioni dello studio includendo potenziali di pregiudizio (imparzialità), le limitazioni del modello animale e le imprecisioni associate ai risultati[2]. c. Descrivere le eventuali implicazioni dei vostri metodi sperimentali o risultati relativamente alla sostituzione, miglioramento e riduzione (le 3R) dell'utilizzo degli animali nella ricerca.
Generalizzazioni/ traslazioni	19	Commentare se, e come, i risultati ottenuti da questo studio possono essere traslati ad altre specie o sistemi, includendo la possibile rilevanza per la biologia umana.
Finanziamenti	20	Elencare tutte le fonti di finanziamento (incluso il numero del contratto) e il ruolo dei finanziatori nello studio.

ARRIVE

The ARRIVE Guidelines: Animal Research: Reporting of *In Vivo* Experiments. Originally published in *PLOS Biology*, June 2010[1]

https://www.nc3rs.org.uk/sites/default/files/documents/Guidelines/ARRIVE%20-%20Italian%20translation.pdf

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Why were the ARRIVE guidelines developed?

- The ARRIVE guidelines were proposed following an extensive review on the reporting of animals in research (Kilkenny et al., 2009). This was the largest survey of the quality of reporting of publically funded animal research in the UK and US.

OPEN ACCESS Freely available online

PLoS one

Survey of the Quality of Experimental Design, Statistical Analysis and Reporting of Research Using Animals

Carol Kilkenny[1*], Nick Parsons[2], Ed Kadyszewski[3], Michael F. W. Festing[4], Innes C. Cuthill[5], Derek Fry[6], Jane Hutton[7], Douglas G. Altman[8]

- The survey identified key areas for improvement:

Experimental design	Statistical analysis	Reporting of studies
Most papers did not report randomisation (88%) or blinding (86%) to reduce bias in animal selection and outcome measurements.	Only 70% of publications fully described statistical methods and presented the result with a measure of variability.	Only 59% included three important pieces of information: hypothesis, number of animals and characteristics of animals.

- The ARRIVE guidelines were created in response to this survey to improve the reporting of animal research.

NC 3Rs

ARRIVE

Why do we need to improve the reporting of animal research?

- Improved reporting is needed to maximise information published and minimise unnecessary animal studies leading to improved translation of pre-clinical research.

- Failures in reporting of animal research have been demonstrated in a variety of research fields.

Cancer

Hess, KR. Statistical design considerations in animal studies published recently in Cancer Research. *Cancer Research* (2011) 71:625.

Stroke

Macleod, MR et al., Systematic review and metaanalysis of the efficacy of FK506 in experimental stoke. *Journal of Cerebral Blood Flow & Metabolism* (2005) 1-9.

Pain

Rice, ASC et al., Animal models and the prediction of efficacy in clinical trials of analgesic drugs: A critical appraisal and call for uniform reporting standards. *Pain* (2008) 139(2):243-7.

Multiple sclerosis

Vesterinen, HM et al., Improving the translational hit of experimental treatments in multiple sclerosis. *Multiple Sclerosis* (2010) 16(9): 1044-55.

NC 3Rs

ARRIVE

Cite this article as: BMJ, doi:10.1136/bmj.39048.407928.BE (published 15 December 2006)

Research

BMJ

Comparison of treatment effects between animal experiments and clinical trials: systematic review

Pablo Perel, Ian Roberts, Emily Sena, Philipa Wheble, Catherine Briscoe, Peter Sandercock, Malcolm Macleod, Luciano E Mignini, Pradeep Jayaram, Khalid S Khan

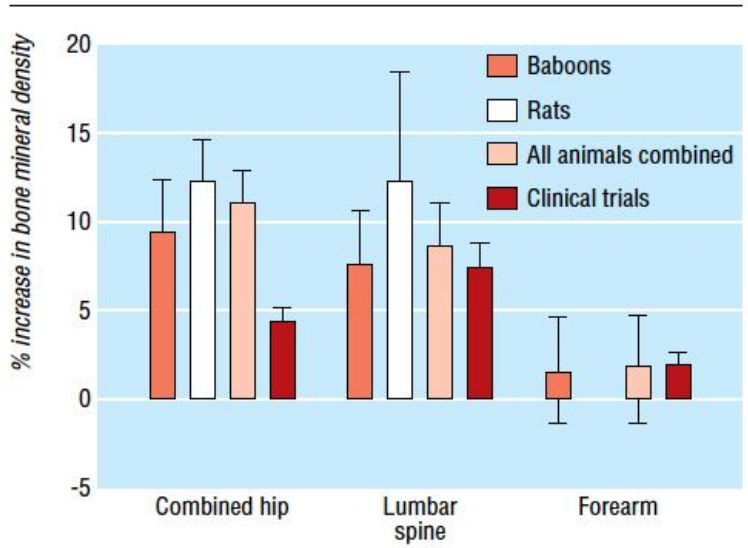


Fig 5 Point estimates and 95% confidence intervals for change in bone mineral density after alendronate administration in baboons, rats, and all animals combined compared with results from clinical trials

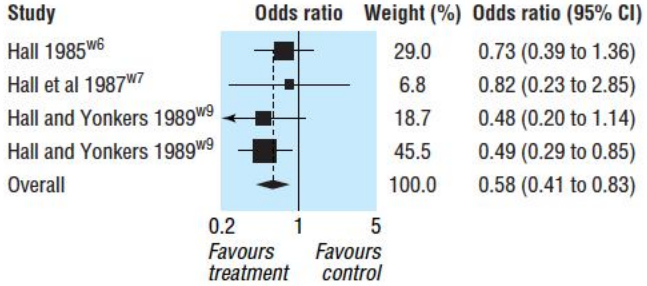


Fig 1 Meta-analysis showing effects of corticosteroids on ability of mice to remain on a taut string (grip test)

Who supports the ARRIVE guidelines?

The ARRIVE guidelines are endorsed by journals, funders and learned societies.

Journals

PLOS

nature

BioMed Central
The Open Access Publisher

eLIFE

Over 400 journals have incorporated the ARRIVE guidelines in their Instructions to Authors

Funders

MRC Medical Research Council

wellcome trust

BBSRC
bioscience for the future

amrc
ASSOCIATION OF MEDICAL RESEARCH CHARITIES

The major funding bodies of biomedical research in the UK support the ARRIVE guidelines.

Universities

MANCHESTER 1824
The University of Manchester

UCL

St George's
University of London

UNIVERSITY OF BATH

Newcastle University

UNIVERSITY OF CAMBRIDGE

CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

Universities endorse the ARRIVE guidelines by encouraging staff and students to use the guidelines.

Learned Societies

BPS BRITISH PHARMACOLOGICAL SOCIETY

SEB
Society for Experimental Biology

SOCIETY OF Biology

British Society for immunology

The Physiological Society

A growing number of learned societies endorse the ARRIVE guidelines and share the guidelines with their members.

NC 3Rs

ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

How can you use the ARRIVE guidelines?

The guidelines can be used when reporting research. In brief, the ARRIVE guidelines include the following:

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

NC 3Rs

For a full description, see the 20-point check list at www.nc3rs.org.uk/ARRIVE

ARRIVE

Why should you use the ARRIVE guidelines?

The ARRIVE guidelines can help the reporting of your research to be:

- Reproducible
- Transparent
- Accurate
- Comprehensive
- Concise
- Logically ordered
- Well written

The ARRIVE guidelines can be used when:

- Writing a manuscript
- Preparing a PhD thesis
- Designing experiments

The ARRIVE guidelines can help promote the 3Rs by ensuring maximal output from animal experiments and reduce the need for excessive animal use.

NC 3Rs

ARRIVE

ITEM		RECOMMENDATION
Title	1	Provide as accurate and concise a description of the content of the article as possible.

EXAMPLE
Thoracic cage plasticity in prepubertal New Zealand white rabbits submitted to T1-T12 dorsal arthrodesis: computed tomography evaluation, echocardiographic assessment and cario-pulmonary measurements. (Canavese et al., 2013).

ITEM		RECOMMENDATION
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.

INTRODUCTION

Background	3	a. Include sufficient scientific background (including relevant references to previous work) to understand the motivation and context for the study, and explain the experimental approach and rationale.
		b. Explain how and why the animal species and model being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.

INTRODUCTION

Objectives	4	Clearly describe the primary and any secondary objectives of the study, or specific hypotheses being tested.

METHODS

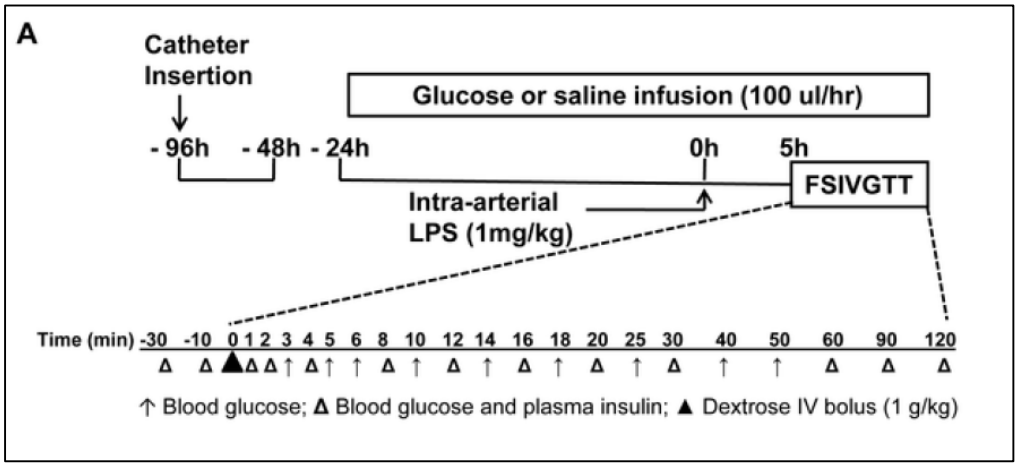
Ethical statement	5	Indicate the nature of the ethical review permissions, relevant licences (e.g. Animal [Scientific Procedures] Act 1986), and national or institutional guidelines for the care and use of animals, that cover the research.

METHODS

Study design	6	For each experiment, give brief details of the study design including: a. The number of experimental and control groups. b. Any steps taken to minimise the effects of subjective bias when allocating animals to treatment (e.g. randomisation procedure) and when assessing results (e.g. if done, describe who was blinded and when). c. The experimental unit (e.g. a single animal, group or cage of animals).

METHODS

Study design	6	d. A time-line diagram or flow chart can be useful to illustrate how complex study designs were carried out.



Chimeric TK-NOG Mice: A Predictive Model for Cholestatic Human Liver Toxicity[S]

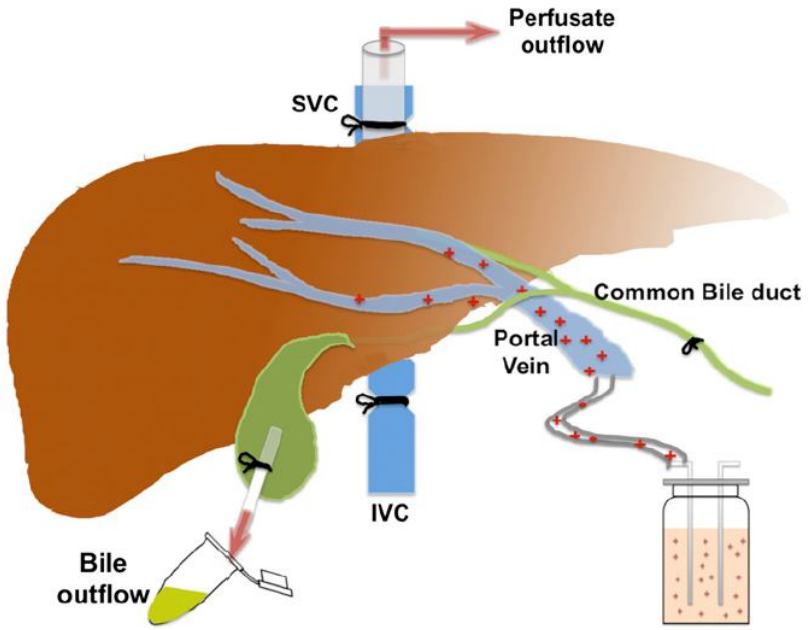


Fig. 2. Diagram of the in situ perfusion system. The liver is continuously perfused with a solution containing 100 μg/ml cefmetazole, which enters the liver via the portal vein. The inferior vena cava (IVC) is ligated, so the perfusate exits via the superior vena cava (SVC) after passing through the liver. The common bile duct is cannulated to direct all bile flow to the gallbladder, which is where the bile is collected.

Xu et al. JPET 2015; 352:274

METHODS

Experimental procedures	7	For each experiment and each experimental group, including controls, provide precise details of all procedures carried out. For example: a. How (e.g. drug formulation and dose, site and route of administration, anaesthesia and analgesia used [including monitoring], surgical procedure, method of euthanasia). Provide details of any specialist equipment used, including supplier(s). b. When (e.g. time of day). c. Where (e.g. home cage, laboratory, water maze). d. Why (e.g. rationale for choice of specific anaesthetic, route of administration, drug dose used).

OPEN

Quality of Methods Reporting in Animal Models of Colitis

Michael Bramhall, MSc, Oscar Flórez-Vargas, MSc,* Robert Stevens, PhD,* Andy Brass, PhD,* and Sheena Cruickshank, PhD†*

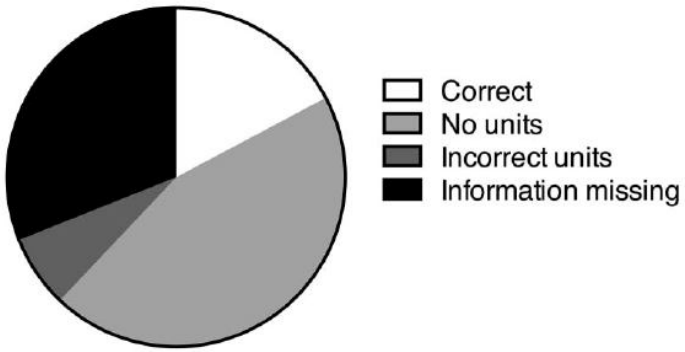


FIGURE 2. Proportion of all DSS articles that correctly and incorrectly described the molecular weight of the DSS used in the experiment. Correct reporting of DSS was only described in 17.24% of articles, and no information at all was provided in 31.03% the studies assessed (n = 29).

Background: Current understanding of the onset of inflammatory bowel diseases relies heavily on data derived from animal models of colitis. However, the omission of information concerning the method used makes the interpretation of studies difficult or impossible. We assessed the current quality of methods reporting in 4 animal models of colitis that are used to inform clinical research into inflammatory bowel disease: dextran sulfate sodium, interleukin-$10^{-/-}$, $CD45RB^{high}$ T cell transfer, and 2,4,6-trinitrobenzene sulfonic acid (TNBS).

Methods: We performed a systematic review based on PRISMA guidelines, using a PubMed search (2000–2014) to obtain publications that used a microarray to describe gene expression in colitic tissue. Methods reporting quality was scored against a checklist of essential and desirable criteria.

Results: Fifty-eight articles were identified and included in this review (29 dextran sulfate sodium, 15 interleukin-$10^{-/-}$, 5 T cell transfer, and 16 TNBS; some articles use more than 1 colitis model). A mean of 81.7% (SD = ±7.038) of criteria were reported across all models. Only 1 of the 58 articles reported all essential criteria on our checklist. Animal age, gender, housing conditions, and mortality/morbidity were all poorly reported.

Conclusions: Failure to include all essential criteria is a cause for concern; this failure can have large impact on the quality and replicability of published colitis experiments. We recommend adoption of our checklist as a requirement for publication to improve the quality, comparability, and standardization of colitis studies and will make interpretation and translation of data to human disease more reliable.

(Inflamm Bowel Dis 2015;21:1248–1259)

METHODS

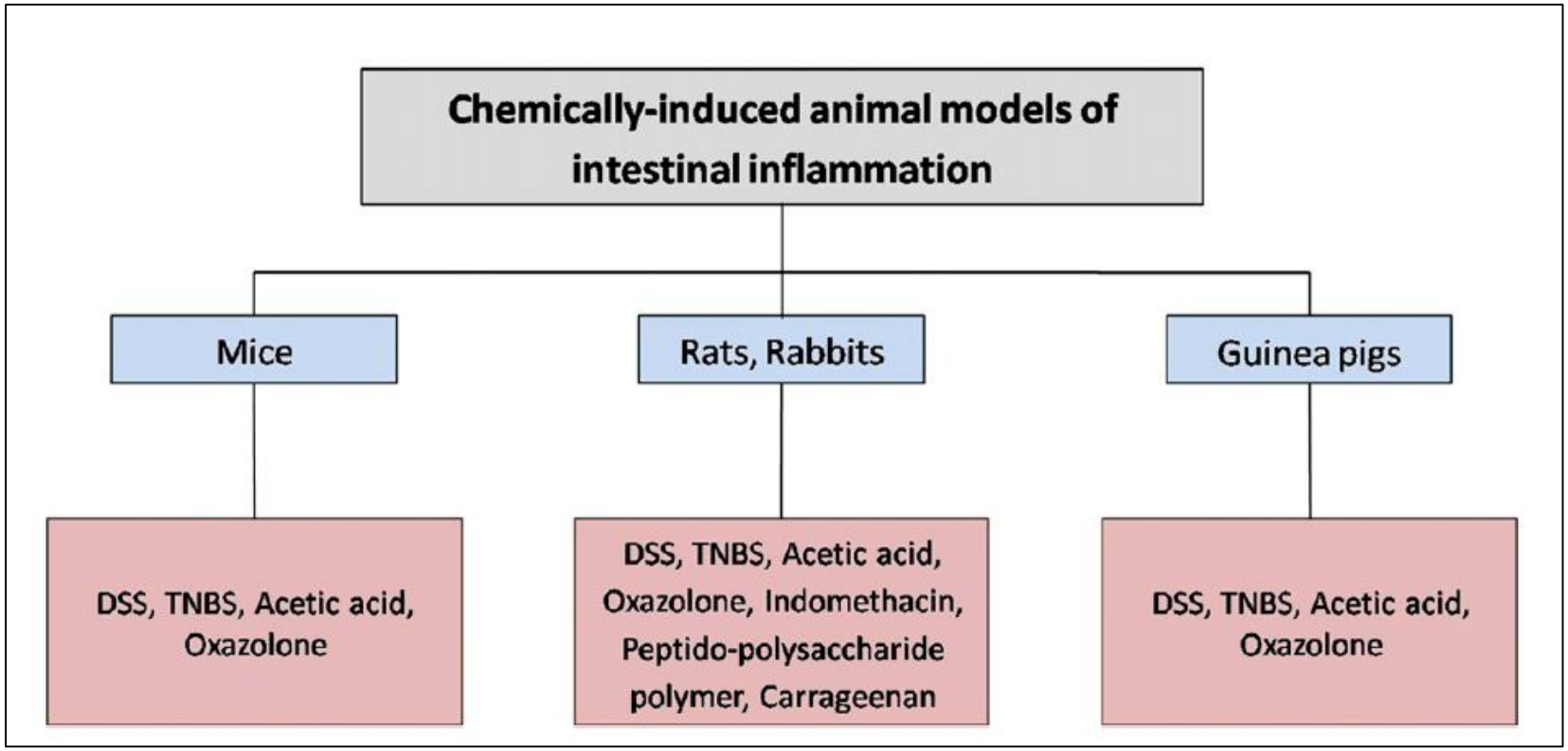
Experimental animals	8	a. Provide details of the animals used, including species, strain, sex, developmental stage (e.g. mean or median age plus age range) and weight (e.g. mean or median weight plus weight range). b. Provide further relevant information such as the source of animals, international strain nomenclature, genetic modification status (e.g. knock-out or transgenic), genotype, health/immune status, drug or test naïve, previous procedures, etc.

Associate Editor: Peter Holzer

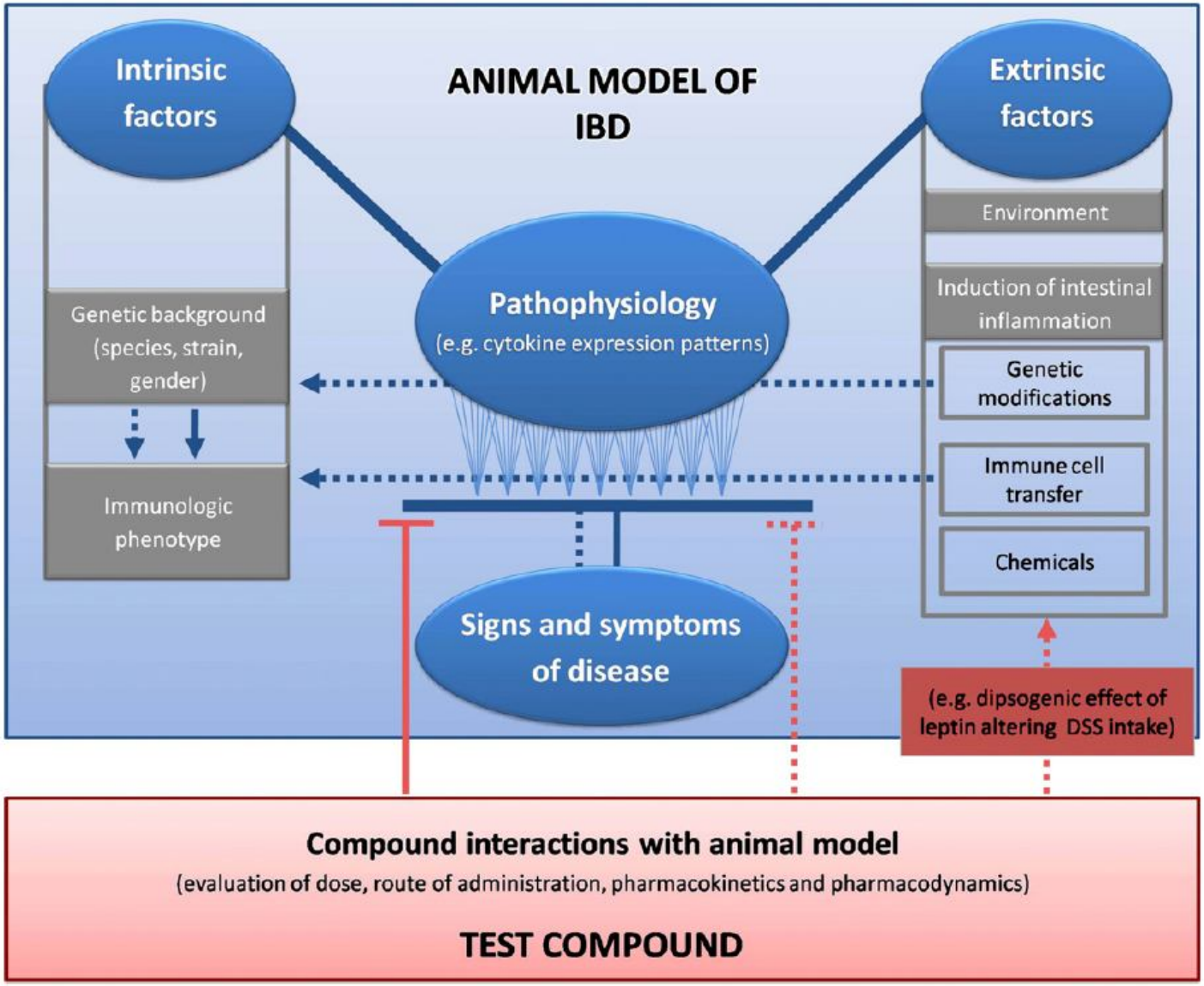
Animal models of chemically induced intestinal inflammation: Predictivity and ethical issues

Giovanni Dothel, Valentina Vasina, Giovanni Barbara, Fabrizio De Ponti *

Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy



Pharmacol Ther 2013;139:71-86.



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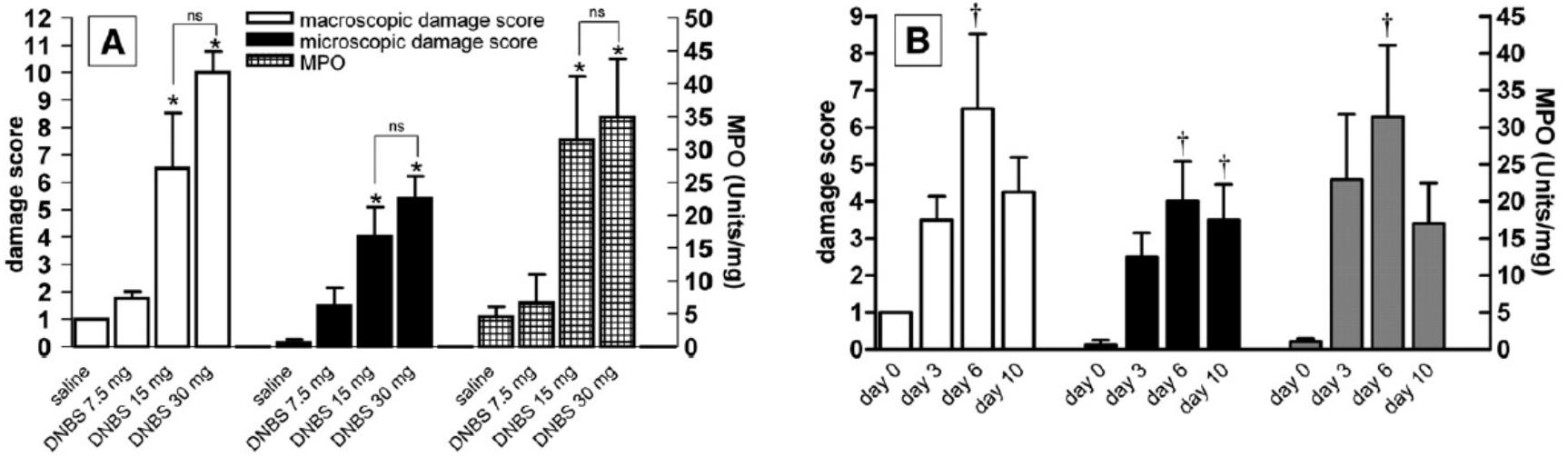
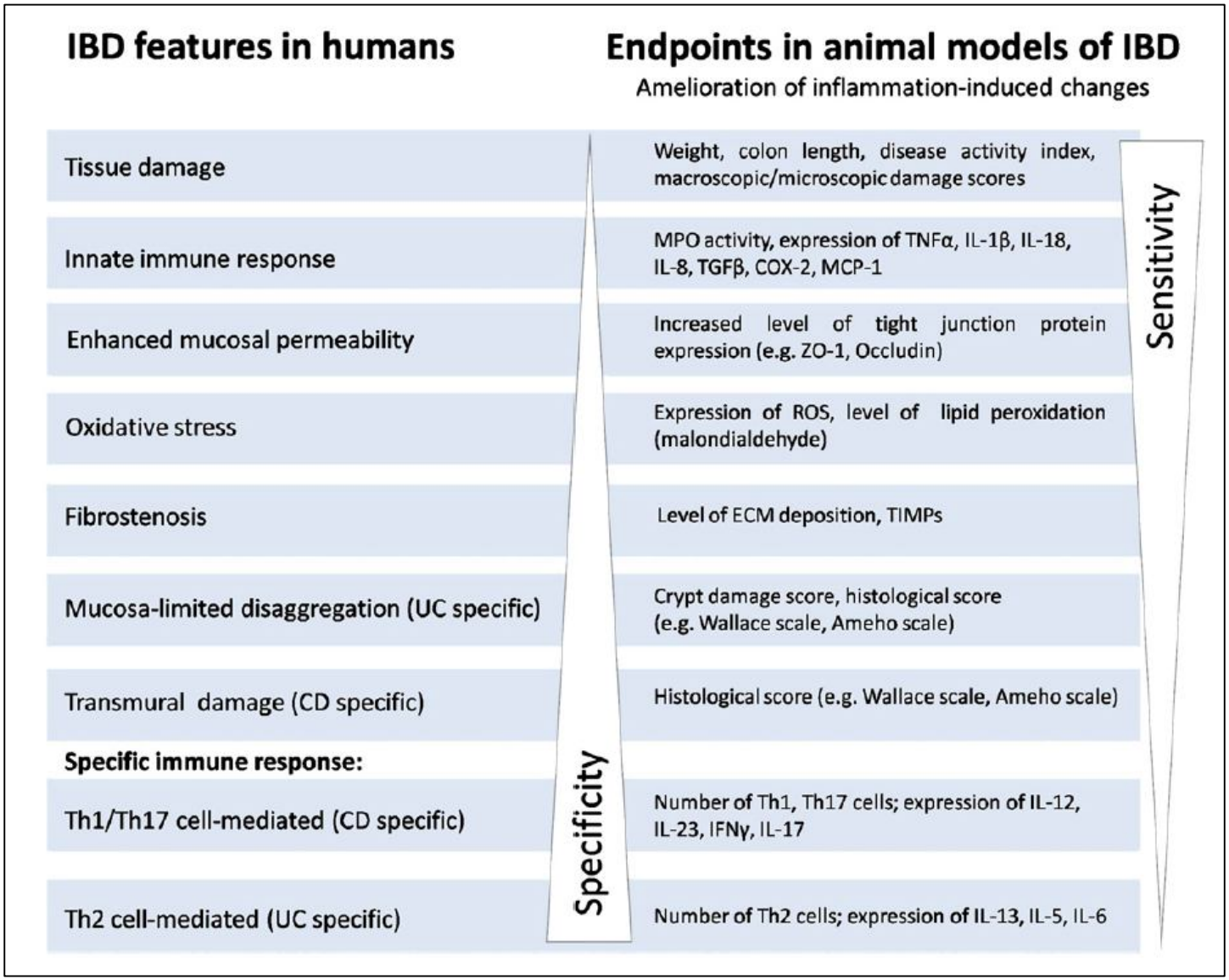
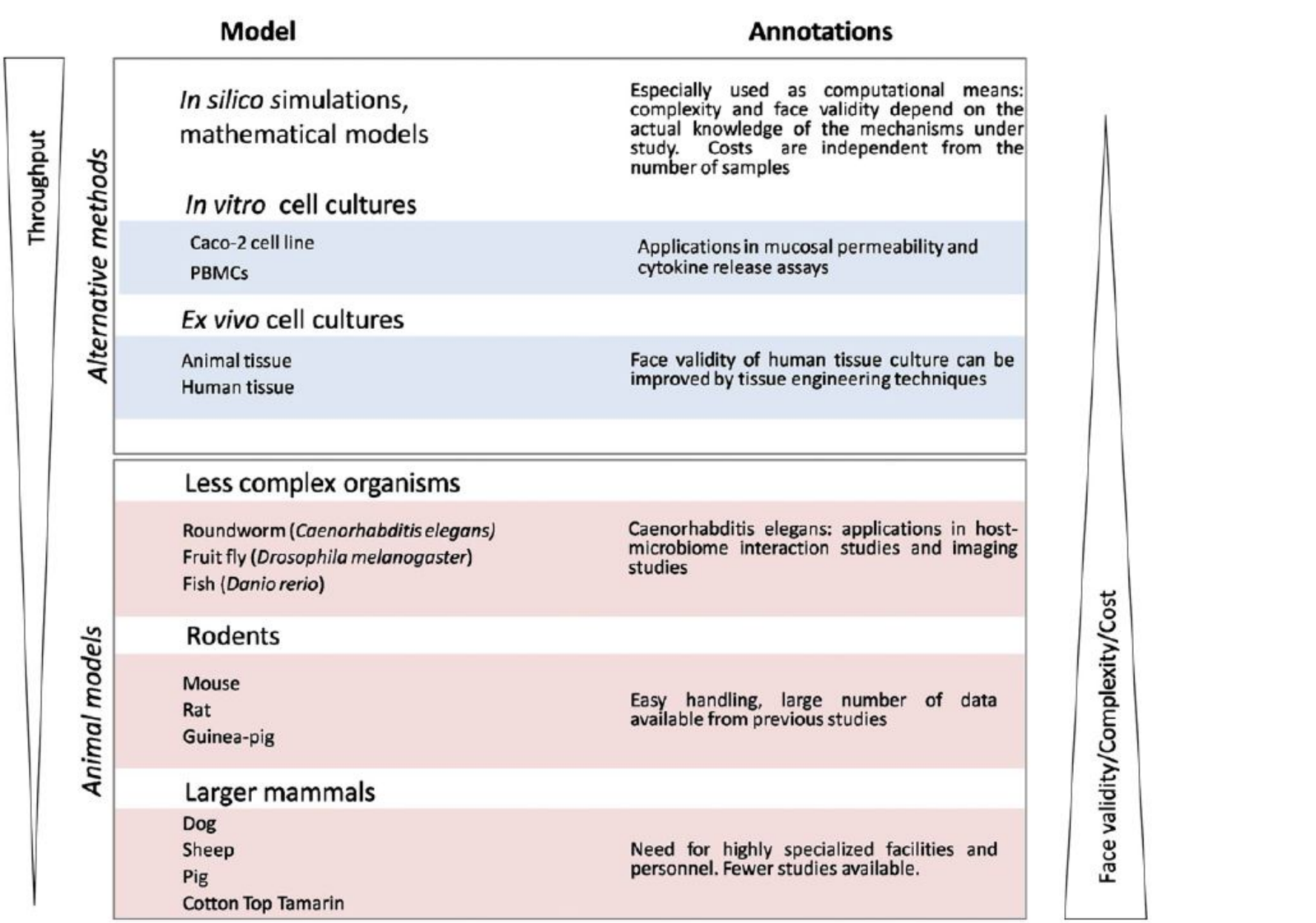


Fig. 6. (A) Dose-dependent effect of different single doses of DNBS in male Sprague Dawley rats (7.5, 15 and 30 mg per rat dissolved in 0.25 mL of 50% ethanol) on macroscopic damage score, microscopic damage score and MPO activity; (B) time course of the effect of 15 mg DNBS (day 3, 6 and 10) on macroscopic damage score, microscopic damage score and MPO activity. Data are expressed as mean values ± SEM; n = 4–8 rats per group. * $P < 0.01$ vs. saline; † $P < 0.05$ vs. saline; ns, not significant. Reproduced, with permission of the copyright holder (John Wiley and Sons), from Vasina et al. (Vasina et al., 2008).

Pharmacol Ther 2013;139:71-86.



Pharmacol Ther 2013;139:71-86.



Pharmacol Ther 2013;139:71-86.

METHODS

Housing and husbandry	9	Provide details of: a. Housing (type of facility e.g. specific pathogen free [SPF]; type of cage or housing; bedding material; number of cage companions; tank shape and material etc. for fish). b. Husbandry conditions (e.g. breeding programme, light/dark cycle, temperature, quality of water etc for fish, type of food, access to food and water, environmental enrichment). c. Welfare-related assessments and interventions that were carried out prior to, during, or after the experiment.

METHODS

Sample size	10	a. Specify the total number of animals used in each experiment, and the number of animals in each experimental group.
		b. Explain how the number of animals was arrived at. Provide details of any sample size calculation used.
		c. Indicate the number of independent replications of each experiment, if relevant

METHODS

Allocating animals to experimental groups	11	a. Give full details of how animals were allocated to experimental groups, including randomisation or matching if done.
		b. Describe the order in which the animals in the different experimental groups were treated and assessed.

METHODS

Experimental outcomes	12	Clearly define the primary and secondary experimental outcomes assessed (e.g. cell death, molecular markers, behavioural changes).

METHODS

Statistical methods	13	a. Provide details of the statistical methods used for each analysis. b. Specify the unit of analysis for each dataset (e.g. single animal, group of animals, single neuron). c. Describe any methods used to assess whether the data met the assumptions of the statistical approach.

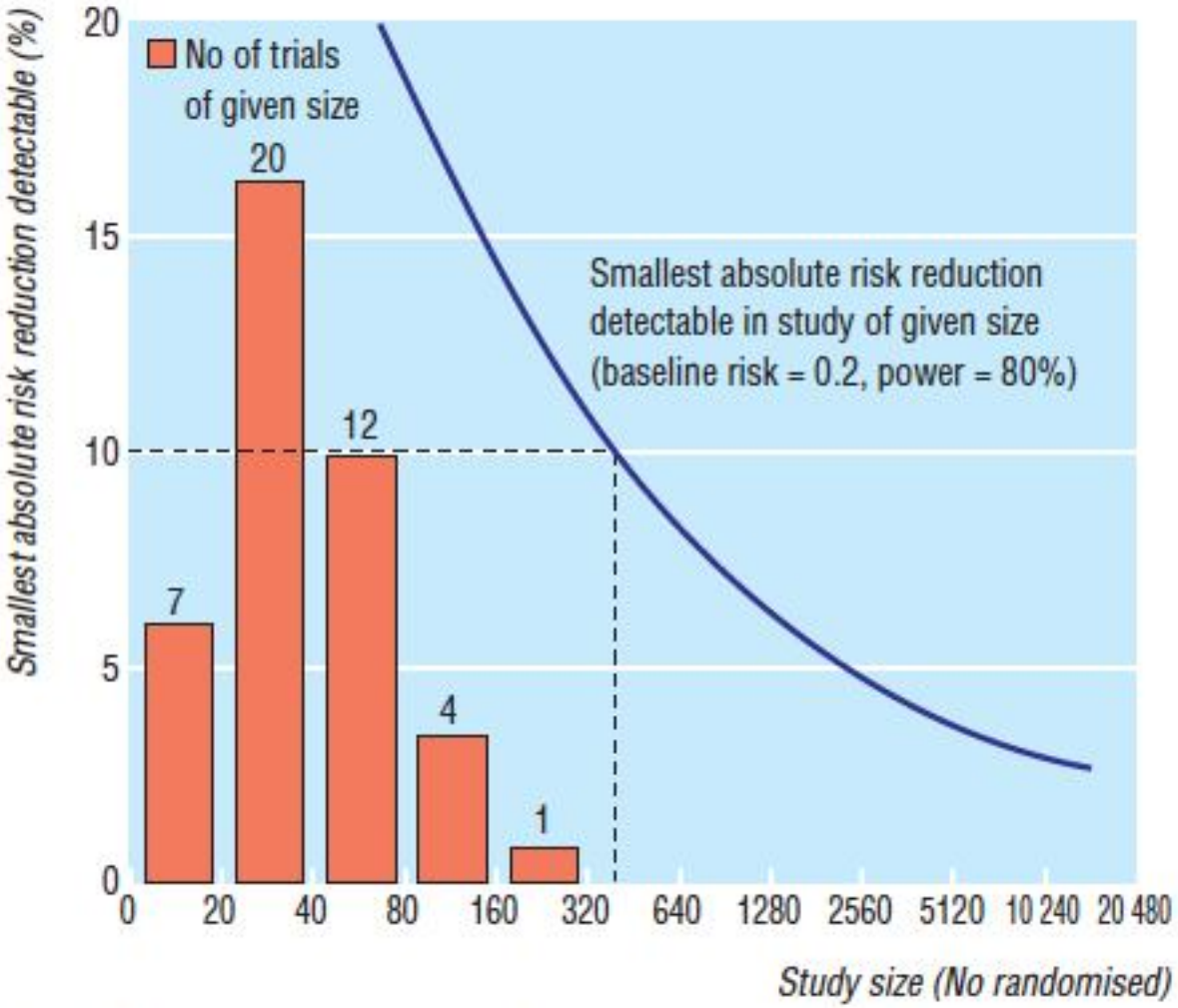


Fig 2 Trial size and smallest absolute risk reduction detectable

RESULTS

Baseline data	14	For each experimental group, report relevant characteristics and health status of animals (e.g. weight, microbiological status, and drug or test naïve) prior to treatment or testing. (This information can often be tabulated).
Numbers analysed	15	a. Report the number of animals in each group included in each analysis. Report absolute numbers (e.g. 10/20, not 50%[2]).
		b. If any animals or data were not included in the analysis, explain why.

RESULTS

Outcomes and estimation	16	Report the results for each analysis carried out, with a measure of precision (e.g. standard error or confidence interval).
Adverse events	17	a. Give details of all important adverse events in each experimental group.
		b. Describe any modifications to the experimental protocols made to reduce adverse events.

DISCUSSION

Interpretation/ scientific implications	18	a. Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature.
		b. Comment on the study limitations including any potential sources of bias, any limitations of the animal model, and the imprecision associated with the results[2].
		c. Describe any implications of your experimental methods or findings for the replacement, refinement or reduction (the 3Rs) of the use of animals in research.

DISCUSSION		
Generalisability/ translation	19	Comment on whether, and how, the findings of this study are likely to translate to other species or systems, including any relevance to human biology.
Funding	20	List all funding sources (including grant number) and the role of the funder(s) in the study.

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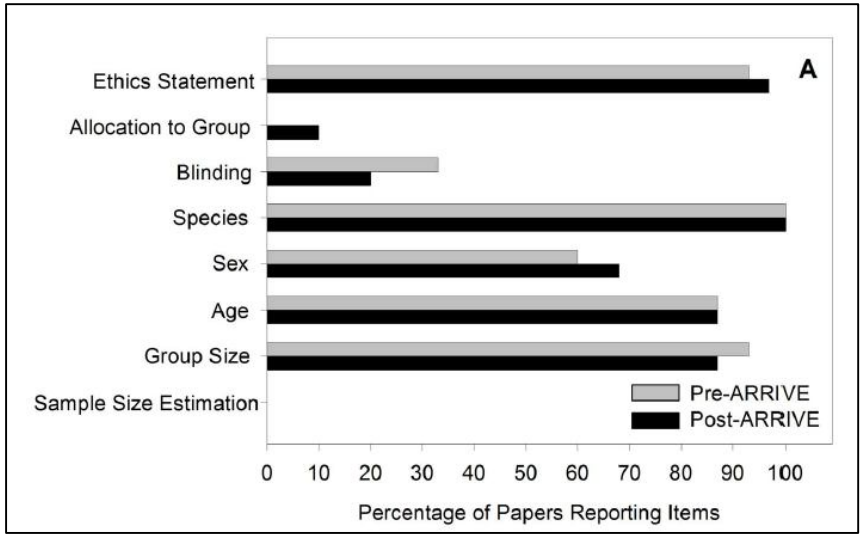
PLOS | BIOLOGY

Perspective

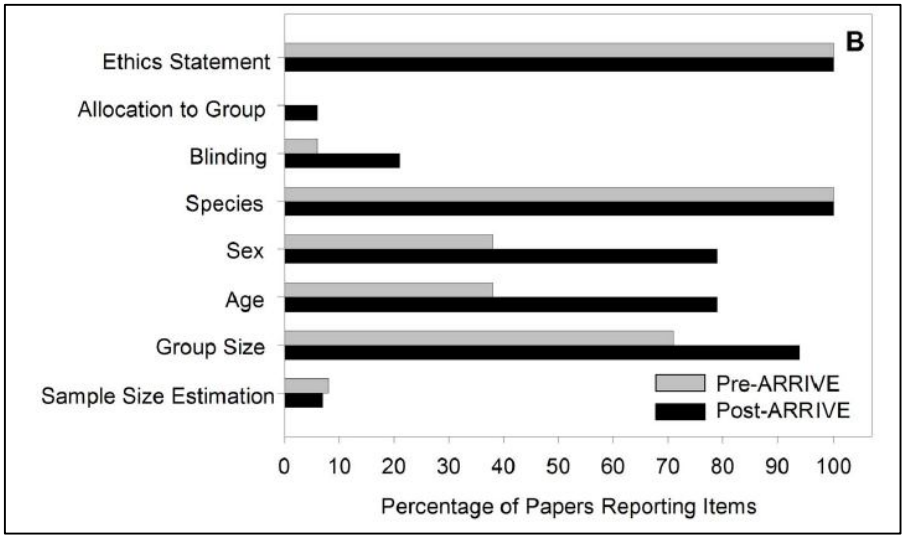
Two Years Later: Journals Are Not Yet Enforcing the ARRIVE Guidelines on Reporting Standards for Pre-Clinical Animal Studies

David Baker[1], Katie Lidster[1]*, Ana Sottomayor[1,2], Sandra Amor[1,3]

1 Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, 2 Escola de Ciências da Saúde, Universidade do Minho, Braga, Portugal, 3 Pathology Department, VU University Medical Centre, Amsterdam, The Netherlands



PLOS journals



Nature journals

Figure 2. Impact of endorsement of ARRIVE guidelines on reporting of EAE studies in PLOS and Nature journals. Papers reporting differences between groups of animals with EAE were assessed over the two years before and the two years after the endorsement of the ARRIVE guidelines. The data show reporting of various aspects of experimental design in (A) PLOS ($n = 46$) and (B) Nature journals ($n = 30$).

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BMJ 2014;348:g3387 doi: 10.1136/bmj.g3387 (Published 30 May 2014)

ANALYSIS

Is animal research sufficiently evidence based to be a cornerstone of biomedical research?

Public acceptance of the use of animals in biomedical research is conditional on it producing benefits for humans. **Pandora Pound** and **Michael Bracken** argue that the benefits remain unproved and may divert funds from research that is more relevant to doctors and their patients

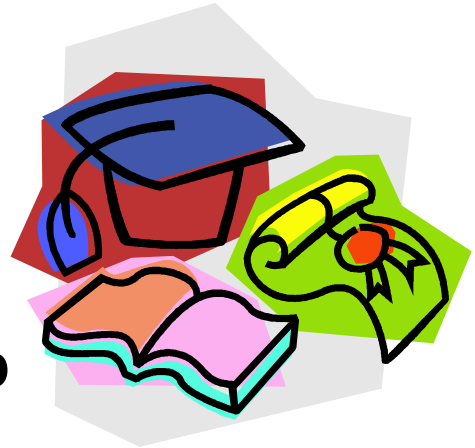
Pandora Pound *medical sociologist*[1], Michael B Bracken *Susan Dwight Bliss professor of epidemiology*[2]

[1]Bath, UK; [2]Yale University Schools of Public Health and Medicine, New Haven CT, USA

Key messages

- The conduct, reporting, and synthesis of much animal research continues to be inadequate
- This current situation is unethical since animals and humans participate in research that cannot produce reliable results
- There is insufficient systematic evidence for the clinical benefits of animal research
- Greater rigour and accountability is needed to ensure best use of public funds

Il RUOLO/LA RESPONSABILITÁ DELL'UNIVERSITÀ



FORMAZIONE

Attività quotidiana: lavoro- ricerca- studio

→ diverse professioni - diverse necessità:

- **studenti**
- **dottorandi**
- **ricercatori**
- **stabularisti**
- **docenti/responsabili di progetti**
- **medici veterinari**

……

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Università di Bologna

Compiti istituzionali dell'Università:

-Didattica

-Ricerca

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Università: partner istituzionale nell'applicazione della Direttiva 2010/63

RICERCA: 3R

Art. 4

Principio della sostituzione, della riduzione e del perfezionamento

1.Gli Stati membri assicurano che, ove possibile, un metodo o una strategia di sperimentazione scientificamente soddisfacente che non comporti l'uso di animali vivi possa essere utilizzato in **sostituzione** di una procedura.

2. ... che il **numero** di animali utilizzati nei progetti sia **ridotto al minimo** senza compromettere gli obiettivi del progetto.

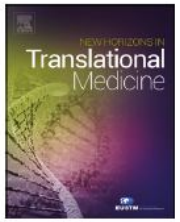
3. ...il **perfezionamento** dell'allevamento, della sistemazione e della cura, e dei metodi usati nelle procedure, eliminando o riducendo al minimo ogni eventuale dolore, sofferenza, angoscia o danno prolungato per gli animali.

New Horizons in Translational Medicine 2 (2014) 5–11

Contents lists available at ScienceDirect

New Horizons in Translational Medicine

journal homepage: www.elsevier.com/locate/nhtm



Research Articles

Animal models in translational medicine: Validation and prediction

Tinneke Denayer, Thomas Stöhr*, Maarten Van Roy

Ablynx NV, Dept. Pharmacology, Zwijnaarde, Belgium

ARTICLE INFO

Available online 27 August 2014

Keywords:
Animal model
Drug development
Translational value
Fit-for-purpose validation

ABSTRACT

Despite large investments in drug development, the overall success rate of drugs during clinical development remains low. One prominent explanation is flawed preclinical research, in which the use and outcome of animal models is pivotal to bridge the translational gap to the clinic. Therefore, the selection of a validated and predictive animal model is essential to address the clinical question. In this review, the current challenges and limitations of animal models are discussed, with a focus on the fit-for-purpose validation. Moreover, guidance is provided on the selection, design and conduct of an animal model, including the recommendation of assessing both efficacy and safety endpoints. In order to improve the clinical translation, the use of humanized mouse models and preclinical applications of clinical features are discussed. On top, the translational value of animal models could be further enhanced when combined with emerging alternative translational approaches.

- Bedside
  Animal models are essential for translation of drug findings from bench to bedside. Hence, critical evaluation of the face and predictive validity of these models is important. Reversely, clinical bedside findings that were not predicted by animal testing should be back translated and used to refine the animal models.
- Benchside
  Proper design, execution and reporting of animal model results help to make preclinical data more reproducible and translatable to the clinic.
- Industry
  Design of an animal model strategy is part of the translational plan rather than (a) single experiment (s). Data from animal models are essential in predicting the clinical outcome for a specific drug in development.
- Community
  Review, standardization and refinement of animal models by disease expert groups helps to improve rigor of animal model testing. It is important that the applied animal models are validated fit-for-purpose according to stringent criteria and reproducible.
- Governments
  As during drug development fit-for-purpose animal models are key for success in clinical translation, financial investments and support from the government to develop, optimize, validate and run such translation tools are important. Over time, this will be of benefit for patients and healthcare institutions.
- Regulatory agencies
  Preclinical testing of a drug in an animal model is not a prerequisite for regulatory agencies before entering clinical trials, but does unquestionably provide valuable data on the expected clinical performance of the drug. Hence, testing in animal models is largely recommended from both a business and patient perspective. In addition, inclusion of safety parameters in animal models will help to build the required safety data package of drugs in development.

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PLOS | MEDICINE

Threats to Validity in the Design and Conduct of Preclinical Efficacy Studies: A Systematic Review of Guidelines for In Vivo Animal Experiments

Valerie C. Henderson[1], Jonathan Kimmelman[1]*, Dean Fergusson[2,3], Jeremy M. Grimshaw[2,3], Dan G. Hackam[4]

1 Studies of Translation, Ethics and Medicine (STREAM) Group, Biomedical Ethics Unit, Department of Social Studies of Medicine, McGill University, Montréal, Québec, Canada, **2** Ottawa Hospital Research Institute, The Ottawa Hospital, Ottawa, Ontario, Canada, **3** Department of Medicine, University of Ottawa, Ottawa, Ontario, Canada, **4** Division of Clinical Pharmacology, Department of Medicine, University of Western Ontario, London, Ontario, Canada

PLoS Med 10(7): e1001489. doi:10.1371/journal.pmed.1001489

Table 4. Most frequent recommendations appearing in preclinical research guidelines for in vivo animal experiments.

Validity Type	Recommendation Category	Examples	*n* (Percent) of Guidelines Citing
Internal	Choice of sample size	Power calculation, larger sample sizes	23 (89)
	Randomized allocation of animals to treatment	Various methods of randomization	20 (77)
	Blinding of outcome assessment	Blinded measurement or analysis	20 (77)
	Flow of animals through an experiment	Recording animals excluded from treatment through to analysis	16 (62)
	Selection of appropriate control groups	Using negative, positive, concurrent, or vehicle control groups	15 (58)
	Study of dose–response relationships	Testing above and below optimal therapeutic dose	15 (58)
Construct	Characterization of animal properties at baseline	Characterizing inclusion/exclusion criteria, disease severity, age, or sex	20 (77)
	Matching model to human manifestation of the disease	Matching mechanism, chronicity, or symptoms	19 (73)
	Treatment response along mechanistic pathway	Characterizing pathway in terms of molecular biology, histology, physiology, or behaviour	15 (58)
	Matching outcome measure to clinical setting	Using functional or non-surrogate outcome measures	14 (54)
	Matching model to age of patients in clinical setting	Using aged or juvenile animals	11 (42)
External	Replication in different models of the same disease	Different transgenics, strains, or lesion techniques	13 (50)
	Independent replication	Different investigators or research groups	12 (46)
	Replication in different species	Rodents and nonhuman primates	8 (31)
Research Program[a]	Inter-study standardization of experimental design	Coordination between independent research groups	14 (54)
	Defining programmatic purpose of research	Study purpose is preclinical, proof of concept, or exploratory	4 (15)

[a]Recommendations concerning the coordination of experimental design practices across a program of research.

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Qualichem *In Vivo*: A Tool for Assessing the Quality of *In Vivo* Studies and Its Application for Bisphenol A

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Abstract

In regulatory toxicology, quality assessment of *in vivo* studies is a critical step for assessing chemical risks. It is crucial for preserving public health studies that are considered suitable for regulating chemicals are robust. Current procedures for conducting quality assessments in safety agencies are not structured, clear or consistent. This leaves room for criticism about lack of transparency, subjective influence and the potential for insufficient protection provided by resulting safety standards. We propose a tool called "Qualichem *in vivo*" that is designed to systematically and transparently assess the quality of *in vivo* studies used in chemical health risk assessment. We demonstrate its use here with 12 experts, using two controversial studies on Bisphenol A (BPA) that played an important role in BPA regulation in Europe. The results obtained with Qualichem contradict the quality assessments conducted by expert committees in safety agencies for both of these studies. Furthermore, they show that reliance on standardized guidelines to ensure scientific quality is only partially justified. Qualichem allows experts with different disciplinary backgrounds and professional experiences to express their individual and sometimes divergent views—an improvement over the current way of dealing with minority opinions. It provides a transparent framework for expressing an aggregated, multi-expert level of confidence in a study, and allows a simple graphical representation of how well the study integrates the best available scientific knowledge. Qualichem can be used to compare assessments of the same study by different health agencies, increasing transparency and trust in the work of expert committees. In addition, it may be used in systematic evaluation of *in vivo* studies submitted by industry in the dossiers that are required for compliance with the REACH Regulation. Qualichem provides a balanced, common framework for assessing the quality of studies that may or may not be following standardized guidelines.

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Table 1. Typology of quality criteria for in vivo studies.

Table 1. Typology of quality criteria for *in vivo* studies.

Class	Quality criteria
Protocol Quality Criteria	
1. Substance	Check of substance properties; check of storage conditions; procedure for obtaining formulations; choice of the control
2. Experimental animals	Correspondence between the characteristics of tested animals and the characteristics of exposed humans; choice of test species/strain; handling of experimental animals; monitoring of experimental animals; monitoring of controls
3. Assay	Sensitivity of the assay; choice of experimental unit; number of groups tested; number of control groups; robustness of regulatory guidelines; test of a single substance or mixture
4. Measured effects	Parameters observed; observation time; biological level observed; precision of effects measurement
5. Tested exposure	Toxicokinetic stage for measuring exposure; level of doses tested; exposure duration; number exposure levels; route of administration; precision of exposure measurement; control of confounders
6. Laboratory procedures and human factors	Experimenter bias
Results Quality Criteria	
7. Results reporting	Results reporting; graphical data representation; abstract vs. raw data
8. Results analysis	Statistical methods used; statistical unit; treatment of data for statistics; statistical power; evaluation of errors, uncertainty, variability
9. Causal interpretation	Interpretation of dose-response; biological mechanism; extrapolation from animals to humans; functional relevance of changes
10. Results interpretation: epistemological context	Epistemological background
11. Results check	Status of peer-review; coherence with literature
12. Results interpretation: expert judgment	Results vs. raw data; assumptions
13. Variability	Variability

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Dissemination of results

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RESEARCH

The association between exaggeration in health related science news and academic press releases: retrospective observational study

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EDITORIAL

Improving the reporting of animal research: when will we ARRIVE?

Nathalie Percie du Sert[1]

"From an author's perspective, applying these guidelines carefully is an opportunity to make the most out of one's own work, ensuring that it provides real value to the scientific landscape and is used by others"

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