

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

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Many factors can influence the outcome and interpretation of experiments using animals – from the strain or sex of the animal through to choosing the correct statistical method for analysis. You would therefore expect such information to be readily available in all publications reporting *in vivo* research, wouldn't you?

However, this is not the case, according to a recent study published by the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs). In the largest survey of its kind, the NC3Rs reviewed 271 publications describing experiments involving rodents and non-human primates in biomedical research; all were publicly funded studies carried out in the US or the UK. Our analysis showed that only 60% of the articles stated the number and characteristics of the animals used (i.e. strain, sex and age or weight). Only 70% of the publications that used statistical methods fully described them and presented the results with a measure of precision or variability. In many papers, it was difficult to assess whether the statistical analysis was appropriate because information detailing the statistical methods was lacking. Most of the papers did not report the use of randomisation (87%) or blinding (86%) to reduce bias in animal selection and outcome assessment (Kilkenny et al., 2009).

Scientific progress relies on adding to the knowledge base by communication within the scientific community, usually through peer-reviewed publication. Failure to report all essential information therefore reduces the utility of the knowledge base that is used to inform subsequent studies, making it difficult to build on or reproduce experiments, allow novel methods to be used or carry out retrospective analyses of data. It also brings into question the peer-review process – the quality control applied by most journals – because scientific rigour cannot be assured if there is not the information to assess whether the experiment was properly designed, executed and analysed.

In the context of animal research, inadequate reporting raises ethical as well as scientific concerns. Incomplete reporting of *in vivo* research might hinder the translation of experimental findings to humans by restricting the potential use of systematic reviews and meta-analyses to assess preclinical evidence. For example, in a meta-analysis looking at animal models of multiple

sclerosis, a substantial number of studies could not be included because results were poorly reported (Vesterinen et al., 2010). There are also concerns that information about the age or sex of the animals used, which should be considered before deciding whether a drug should progress to clinical trials, especially if the condition that the drug is proposed to treat is gender specific or affects a particular age class, is not readily reported. Missing information reduces the value gained from animal experiments, which can result in unnecessary additional studies and financial expense – neither of which is desirable, particularly in the current climate.

ARRIVE-ing at a solution

So, what is the solution? The NC3Rs recently published new guidelines aimed at providing a steer to improve the reporting of animal experiments (Kilkenny et al., 2010). The guidelines, called ARRIVE (Animal Research: Reporting of *In Vivo* Experiments), were developed and 'road tested' in collaboration with scientists, statisticians, journal editors and research funders, and consist of a

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checklist of 20 items that represent the key information that is necessary to describe a study in a comprehensive and transparent manner. The ARRIVE guidelines cover the main aspects of a scientific publication and make recommendations on the reporting of the study design, experimental procedures, animal characteristics, housing and husbandry, and statistical analysis. 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.

The intention of ARRIVE is to maximise the output of research that uses animals. Achieving this will benefit the whole scientific community. The success of such an approach has already been demonstrated for clinical research, where guidelines were developed to address concerns regarding the poor reporting of randomised control trials (RCTs) (Moher et al., 1994). The so-called CONSORT statement (Begg et al., 1996; Schulz et al., 2010) was drafted by an expert working group composed of editors, clinical epidemiologists and statisticians, and was subsequently endorsed by many journals. These guidelines have contributed significantly to improving RCT reports (Plint et al., 2006).

Evolution and impact of ARRIVE

The ARRIVE guidelines were simultaneously published in eight bioscience journals in 2010 and, since then, almost 40 journals have adopted them (the full list can be found on the NC3Rs website at <http://www.nc3rs.org.uk/ARRIVE>), e.g. by including a link to the guidelines in their instructions to authors. A study looking at the impact of CONSORT two years following its publication found

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that, even though all journals that were analysed had improved reporting of RCTs over time, reporting quality was significantly higher in journals that had endorsed the reporting guidelines (Moher et al., 2001). This is our objective with the ARRIVE guidelines: we will assess whether and how they change the reporting of animal research in the next few years. There are, of course, hundreds of bioscience journals worldwide, and there is a long way to go in terms of our ambition of universal support and uptake.

The ARRIVE guidelines were developed as a consensus and should evolve as a consensus. As such, experience and feedback are essential in determining whether they should be improved and, if so, how. The impact and evolution of the ARRIVE guidelines rests on the collective efforts of authors, peer reviewers, journal editors, publishers and funding bodies to disseminate, endorse and apply them. To do otherwise should be unsustainable at a time when there is increased pressure on resources and a greater expectation that research will be exploited.

REFERENCES

- Begg, C., Cho, M., Eastwood, S., Horton, R., Moher, D., Olkin, I., Pitkin, R., Rennie, D., Schulz, K. F., Simel, D. et al. (1996). Improving the quality of reporting of randomized controlled trials. The CONSORT statement. *JAMA* **276**, 637-639.
- Kilkenny, C., Parsons, N., Kadyszewski, E., Festing, M. F., Cuthill, I. C., Fry, D., Hutton, J. and Altman, D. G. (2009). Survey of the quality of experimental design, statistical analysis and reporting of research using animals. *PLoS ONE* **4**, e7824.
- Kilkenny, C., Browne, W. J., Cuthill, I. C., Emerson, M. and Altman, D. G. (2010). Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research. *PLoS Biol.* **8**, e1000412.
- Moher, D., Dulberg, C. S. and Wells, G. A. (1994). Statistical power, sample size, and their reporting in randomized controlled trials. *JAMA* **272**, 122-124.
- Moher, D., Jones, A. and Lepage, L. (2001). Use of the CONSORT statement and quality of reports of randomized trials: a comparative before-and-after evaluation. *JAMA* **285**, 1992-1995.
- Plint, A. C., Moher, D., Morrison, A., Schulz, K., Altman, D. G., Hill, C. and Gaboury, I. (2006). Does the CONSORT checklist improve the quality of reports of randomised controlled trials? A systematic review. *Med. J. Aust.* **185**, 263-267.
- Schulz, K. F., Altman, D. G. and Moher, D. (2010). CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* **340**, c332.
- Vesterinen, H. M., Sena, E. S., French-Constant, C., Williams, A., Chandran, S. and Macleod, M. R. (2010). Improving the translational hit of experimental treatments in multiple sclerosis. *Mult. Scler.* **16**, 1044-1055.

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