Editorial

JBJS Will Require Adherence to ARRIVE Guidelines for Animal Research to Reduce Bias and Improve Quality of Reporting

A fundamental premise of scientific research is that publications should provide enough information for the study to be replicated, but as research methodologies become more complex, ensuring research rigor and reproducibility is increasingly difficult. Important details are often omitted from submitted manuscripts, and these deficiencies are sometimes not recognized during peer review. For example, a recent survey of published research using laboratory animals found that only 59% of the studies stated a hypothesis, and 4% failed to indicate the number of animals used[1]. Failure to adequately describe methodology has scientific, ethical, and financial implications, and this is especially true for animal research.

The CONSORT (Consolidated Standards of Reporting Trials) statement[2,3] was developed to provide researchers and reviewers guidance about appropriate content in randomized clinical trials, and many journals, including JBJS, encourage authors to follow those guidelines. Building on the success of the CONSORT statement for human clinical studies, the ARRIVE (Animal Research: Reporting of In Vivo Experiments) guidelines[4] were developed for animal research. They aim to improve research quality, reduce bias in reporting, improve generalizability, and minimize unnecessary studies.

Specifically, the ARRIVE guidelines "consist of a checklist of 20 items describing the minimum information that all scientific publications reporting research using animals should include, such as the number and specific characteristics of animals used (including species, strain, sex, and genetic background); details of housing and husbandry; and the experimental, statistical, and analytical methods (including details of methods used to reduce bias such as randomisation and blinding). All the items in the checklist have been included to promote high-quality, comprehensive reporting to allow an accurate critical review of what was done and what was found."[4] (Fig. 1).

Joining the nearly 600 journals that have endorsed these guidelines[5], JBJS is adopting the requirement that all manuscripts reporting on animal research include an annotated checklist of the ARRIVE guidelines. We recognize that some studies will be pilot or hypothesis-generation studies, but authors should report as much relevant information as possible. We also recognize that the JBJS word limit precludes including all of the details from the guidelines in the text, and therefore authors are welcome to provide additional data in an online-only appendix upon submission. We intend to make the completed ARRIVE checklist available to reviewers and editors during the review process. This change will be effective on January 1, 2020.

Anticipating the inclusion of the ARRIVE guidelines in the published results, authors may want to consider those guidelines when proposing and initiating in vivo animal research studies. To improve overall design, a companion guideline, PREPARE (Planning Research and Experimental Procedures on Animals: Recommendations for Excellence)[6] is available and includes ethical and logistical topics that authors should consider when planning animal studies. In addition, as the ARRIVE guidelines are revised, we will provide the updated information to authors.

The important issue of bias against publishing negative findings has been addressed in human clinical research by mandatory prospective registration of clinical trials. The nature of preclinical animal research does not lend itself to this level of formality, but JBJS recognizes its role in encouraging the publication of both positive and negative findings. JBJS will encourage reviewers to avoid bias against negative results in well-designed studies.

Simply instituting a requirement to follow the ARRIVE guidelines will not ensure adherence by authors or reviewers. For example, a review of randomly selected papers in a journal that endorsed the guidelines found that one-half to two-thirds of publications omitted basic ethical, demographic, and baseline descriptive data[7]. Similarly, a survey of Swiss researchers

Disclosure: On the **Disclosure of Potential Conflicts of Interest** forms, *which are provided with the online version of the article*, one or more of the authors checked "yes" to indicate that the author had a relevant financial relationship in the biomedical arena outside the submitted work (http://links.lww.com/JBJS/F523).

	ITEM	RECOMMENDATION
TITLE	1	Provide as accurate and concise a description of the content of the article as possible.
ABSTRACT	2	Provide an accurate summary of the background, research objectives (including details of the species o 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 understanc 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 objective and, where appropriate, the study's relevance to human biology.
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
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). A time-line diagram or flow chart can be useful to illustrate how complex study designs were carried out
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 specialis 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).
Experimental animals	8	a. Provide details of the animals used, including species, strain, sex, developmental stage (e.g., mean o 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.
Housing and husbandry	9	Provide details of: a. Housing (e.g., 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 before, during, or after the experiment.
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 decided. Provide details of any sample size calculation used c. Indicate the number of independent replications of each experiment, if relevant.
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.
Experimental outcomes	12	Clearly define the primary and secondary experimental outcomes assessed (e.g., cell death, molecular markers, behavioural changes).
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.
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) before 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%[a]). b. If any animals or data were not included in the analysis, explain why.
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[a]. 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.
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.

[a]Schulz, et al. (2010) [24].
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Fig. 1

ARRIVE guidelines for reporting in vivo animal research. (Reproduced, under Creative Commons Attribution License 4.0, from: Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG. Improving bioscience research reporting: the ARRIVE guidelines for reporting animal research. PLoS Biol. 2010 Jun 29;8[6]: e1000412.)

involved in animal research found that one-half of the authors whose last publication was in a journal requiring use of the ARRIVE guidelines were unaware of the guidelines[8]. Successful implementation of the ARRIVE guidelines will require the input of both authors and reviewers, but we anticipate that adopting this standard will help improve the validity, reproducibility, and impact of our publications. ■

Thomas W. Bauer, MD, PhD
Joan E. Bechtold, PhD
Marc F. Swiontkowski, MD

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