



# Commentary on Adherence to ARRIVE Guidelines in Chinese Journal Reports on Neoplasms in Animals

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## Introduction

Animal experiment, an important means and basic approach for biomedical research, serves as a bridge connecting fundamental research and clinical trials [1] and also is one of the most controversial fields in scientific community [2]. The basic goal of pre-clinical animal experiment lies in primarily verifying the safety and effectiveness of intervention measures, and its result is the direct evidence to determine whether or not new intervention measures should enter clinical research stage and further design clinical trial, so as to protect the volunteers of phase I clinical experiment [1].

With rapid development of various fields in social sciences in 1960s, the number of medical researches including animal experiment had soared in the latter half of the 20<sup>th</sup> century [3]. For the database of PubMed only, the new published papers on a monthly basis reached 63,000 [4]. However, there were many defects in the quality of published medical research reports. Research results with incomplete report information can make the obtainment of scientific information extremely difficult or even be misleading, hence influencing the effective utilization of themselves [2] and causing waste to input capital and experiment animal, which could have been avoided. Therefore, in using animals for fundamental research, especially animal experiment financed by important funds, researchers are responsible for objectively, completely and clearly report how the experiment is designed, executed and evaluated.

The problem of incompleteness of medical research report had been paid attention to by scholars as early as at the end of the 20<sup>th</sup> century. In 1996, the statement of Consolidated Standards of Reporting Trials (CONSORT), the only unified standard for randomized controlled experiment report, was published, and it was prepared by an international team of clinical experiment experts, statisticians, epidemiologists and bio-medical journal editors, with a view to improving report quality of randomized controlled trials (RCT) [5]. In the following decade, over 90 types of various health and hygiene related report guidelines had been issued, involving clinical research, fundamental research and systemic review and etc. Data showed that the application of medical report norms was helpful for improving medical research report quality and methodological quality [6,7].

In 2010, Animal Research: Reporting: In Vivo Experiments Guidelines (ARRIVE Guidelines) [8] and Gold Standard Publication Checklist (GSPC) [9] were published in succession, laying the foundation for standardizing animal experiment for improving animal

experiment report quality. In May 2016, the paper Adherence to ARRIVE Guidelines in Chinese Journal Reports on Neoplasms in Animals was published on Plos One, in which the author evaluated the quality of reports on neoplasms area animal experiment financed by National Natural Science Foundation of China (NSFC) published on Chinese journals on the basis of ARRIVE Guidelines [10].

## ARRIVE Guidelines

### Why and how to prepare ARRIVE guidelines?

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) organized one animal experiment report quality survey, finding out that most journals failed to completely report the key information of how to design, execute and analyze experiment research [11-14].

To uplift animal experiment report quality, promote animal research standardization and transparency, and ensure complete evaluation and utilization of animal experiment materials to avoid unnecessary waste of experiment animal, NC3Rs advocated to prepare a report guideline for animal research based on CONSORT statement [15,16], namely ARRIVE Guidelines [8], hence providing reference foundation for producers, users and peer review experts of animal experiment.

Same as medical report guidelines like CONSORT statement, the expert team composition for ARRIVE Guidelines preparation displayed internationalization and multidisciplinary features, for it included researchers, statisticians, journal editors and financiers from different fields [8]. In 2010, the ARRIVE Guidelines developed by NC3Rs was published on journals, such as, PLoS Biology [8], Journal of Gene Medicine, Experimental Physiology, Journal of Physiology, British Journal of Pharmacology and Laboratory Animals, attracting wide attention and support from the medical circle.

### What is the status of animal experiment report quality?

ARRIVE Guidelines provided reference foundation for animal experiment report quality baseline surveying. Liu YL et al. retrieved in two main Chinese databases and evaluated the information of 396 neoplasms animal experiment reports [10]. Results showed that key information like research design and results were incomplete; the report rate of ARRIVE Guidelines item in half of them was less than 50%, including 3b in introduction preface, 5, 6d, 7c, 7d, 9a, 9b, 9c, 10b, 10c, 11a, 13b and 13c in methodologies, 14, 15a, 15b, 17a and 17b in

results, and 18b, 18c and 19 in discussion and conclusion [10]. Especially, no research had used isochrones map or flowchart to explain the complex research design, not to mention calculation for sample size needed for animal experiment. Items with low report rate should be the link to be paid attention to and enhanced for researchers in design, execution and report of animal experiment. Results of incomplete animal experiment report could also be seen in other researches [17-20]. Due to lack of key information of design, execution and data analysis, research results of animal experiments were hard to explain and repeat, significantly limiting the application of these fundamental researches into future scientific studies and policy making.

There are many reasons for the incomplete animal experiment report information evaluated herein. The first researcher is likely to pay more attention to the design of fundamental research to the neglect of report link, while the second researcher has not noticed and used animal experiment report standards. Hence, the promotion of ARRIVE Guidelines and GSPC has to be enhanced, so that more fundamental researchers can get to know and apply them.

### Where to obtain and apply ARRIVE guidelines?

NC3Rs provides relatively rich ARRIVE Guidelines information resources ([www.nc3rs.org.uk/ARRIVE](http://www.nc3rs.org.uk/ARRIVE)), including free download of the full text and relevant information, not to mention the translated versions in six languages of Chinese, Italian, Japanese, Portuguese, Portuguese (Brazilian) and Spanish for the convenience of readers (Figure 1).

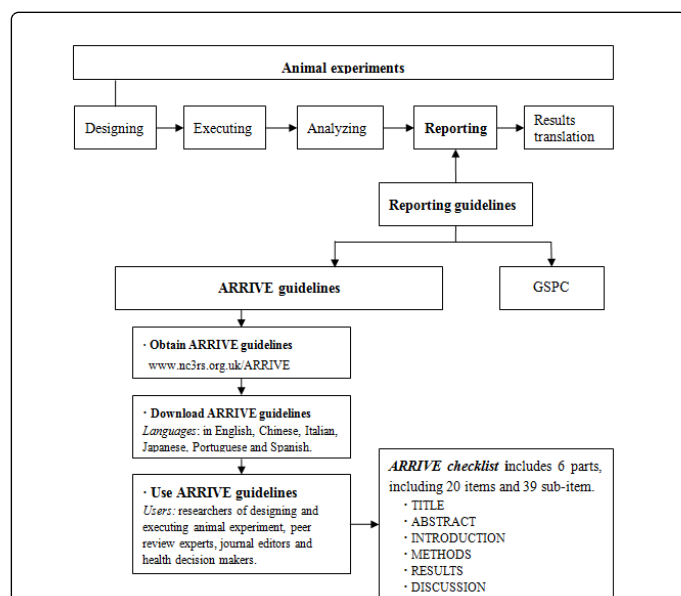


Figure 1: A flow diagram about the use of ARRIVE guidelines.

Correct use of ARRIVE Guidelines can ensure objective and complete report of animal experiment execution method, time, place and causes as far as possible, not only reducing excessive use of experiment animal, ensuring experiment repeatability, but also providing reference foundation for clinical trials knowledge translation, transition and utilization of animal experiment.

### What contents does ARRIVE guidelines have?

ARRIVE Guidelines includes 6 parts of “title, abstract, introduction preface, methods, results and discussions”, including 20 items and 39 sub-item, involving important information of animal number and features (like species, strain, sex, developmental stage type, species, gender and gene), housing residence and husbandry conditions feeding, experiment, statistical and analytic methods (including use of randomisation procedure and blind method to reduce bias) and making simple explanation to each item [8]. The evaluation content is all necessary information that should be reported by animal experiment.

### GSPC

#### Why and how to prepare GSPC?

Conclusions obtained in pre-clinical evaluation (mainly animal experiment) serve as one of the foundations for evidence-based decision making. Systemic review of animal experiment has become a new trend in pre-clinical research [21]. Systemic review with proper analyses could soundly evaluate whether to conduct clinical trials [22]. However, animal experiment with low report quality would severely influence systemic review accurate judgment of research quality. High report quality is not equal to high methodological quality, but it can bring huge obstacles for readers in understanding research authenticity and practicality [1], causing huge waste of fundamental experiment research resources. The development of animal experiment systemic review is not only determined by its own methodological development but also limited by improvement of animal experiment report quality.

To improve animal experiment quality and promote further development of review, 15 experts from different disciplines at Nijmegen Medical Centre of Radboud University designed and formulated the GSPC [9].

#### What are the contents of GSPC?

GSPC was published on Alternatives to Laboratory Animals (ATLA) in May 2010, including introduction, methods, results and discussion and consisting of 54 items in 11 aspects, with many of them having 1 to 10 specifications for supplementary explanation [9]. Its formulation was also based on literature review and existing scientific evidence results, including important information like objective and complete report experimental design, animal feeding environment (including temperature, humidity, ventilation and lighting) and rising.

#### Comparison of ARRIVE guidelines and GSPC

For ARRIVE Guidelines and GSPC, they have major differences in terms of number of evaluation items, but the core evaluation contents vary little, both including report highlights in animal experiment. It was pointed out that GSPC had too many specifications, which, however, did not influence the interest of users [23]. Compared with ARRIVE Guidelines, report items listed in GSPC were more specific, including feeding place (humidity, ventilation, lighting, noise and cage), nutrition (food type, composition and feeding regimes) as well as water information. The above experiment design and execution details are more helpful for objectively and fully understanding specific experiment processes for readers, improving animal experiment repeatability, and avoiding the overuse of experiment animal. Besides, GSPC highlights the basic rationale behind animal feeding conditions

and reporting animal experiment design [24]. Whether ARRIVE Guidelines or GSPC, they both have provided sound reference foundation for animal experiment design, execution, report, evaluation, and transformation.

At present, most scholars hold that the goal of ARRIVE Guidelines and GSPC lies not in compulsively standardizing research report structure, but in providing referable checklist for users (ARRIVE Guidelines target), so as to ensure full evaluation and utilization of information provided by animal experiment and promote information completeness and transparency in fundamental research [8]. The subject of animal experiment report quality guidelines/checklist not only includes researchers of designing and executing animal experiment but also peer review experts, journal editors and health decision makers. Promoting the improvement of animal experiment report quality needs the joint efforts of authors, editors, reviewers and research financiers [8]. Sound use of ARRIVE Guidelines and GSPC, not only promotes the design, execution and analysis of animal experiment more completely and objectively, but also uplifts the overall level of research papers and journals on animal research, and facilitates the development of systemic review of animal experiment. We intensively call for quick introduction of ARRIVE Guidelines and GSPC into biological journals instructions preparation, so as to control the quality of papers before publication, uplift paper design, execution, report quality and biomedical journal quality, and thus optimize research result benefits.

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