《中国中西医结合杂志》动物实验报告清单请参考 ARRIVE 指南（Bilingual version）

以下指南正文来源：arriveguidelines.org

NC3Rs National Centre for the Replacement Refinement & Reduction of Animals in Research

中文版

ARRIVE 指南 2.0

动物实验：体内实验的报告

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ARRIVE指南2.0版是发表动物实验研究报告的内容清单，于2020年7月在*PLOS Biology*杂志上发表。这份清单确保动物实验的研究报告具备足够的研究细节，以增加相关的知识内容。研究报告的透明化，能使读者和审稿人充分地审查研究内容，评估研究方法学的严谨性，以重复研究的方法或结果。

提高动物实验研究的透明化程度——为什么是ARRIVE?

围绕动物实验研究的可重复性问题，引起了科学家、基金资助方和政策制定者的极大关注。

透明和准确的报告是研究可重复的基石。它使得研究可以被有效地评估，从而为未来的研究、政策和临床实践提供信息。

然而，动物实验研究结果发表时常缺乏重要信息，这妨碍了对研究方法和结果的充分评估。为了解决这一问题，ARRIVE指南最先在2010年发表。更新后的指南——ARRIVE 2.0在2020年发布，同时还发布了一份可以提供更多背景信息的解释与说明文件。

ARRIVE 2.0简介

ARRIVE2.0是广泛国际协作的结果，其研发过程审慎地考虑和采纳了来自科学界的意见和建议。本指南的作者包括基金资助方、期刊编辑、方法学家、统计学家和来自学术界和企业界的研究人员。通过德尔菲调查，收集了更多的来自其他外部利益相关方的意见和建议。指南撰写的研究人员，还对这一指南进行了实地测试，以确保其可以在实践中被充分理解和应用。

本指南适用于任何与活体动物相关的研究，从哺乳动物到鱼，也包括无脊椎动物，涉及了生命科学全链条。

为了确保最关键的问题最先被关注到，这部指南的清单条目按优先级划分为了两部分，每一部分的条目之间没有等级之分。两部分清单详见后页。在动物实验研究报告中，充分报告两部分内容是最佳的。

如何使用本指南

指南在整个动物实验研究过程中都是有用的：

- 在动物实验研究的计划期间：指南及其解释与说明文件，对活体动物实验的设计、减少偏倚、样本量估算以及统计分析等方面提供了建议，以帮助研究人员设计严谨和可靠的实验。
- 在动物实验研究的实施期间：参考指南有助于让研究人员将研究方法的重要信息记录下来，这些信息将在后期稿件撰写时有用。
- 撰稿时：可以使用指南及其解释与说明文件作为备忘，确保稿件包含了所有的相关信息。
- 审稿时：可以使用指南及其解释与说明文件，确保所有研究相关的信息都具备，以评价该研究。

支持使用ARRIVE 2.0的相关资源

在www.ARRIVEguidelines.org上可以找到各种各样的资源。包括：

- 我们对指南每个条目进行了解释与说明。这些解释与说明包括对动物实验研究的广泛性建议，指南每个条目设立的理由和证据，也给出了发表文献中良好报告的清晰示例。
- 可填写的ARRIVE2.0清单。可填写的清单能够使研究人员表明稿件中与每个条目相关信息在稿件的具体位置。我们提供两种清单，一种是ARRIVE关键10条，另一种是完整的ARRIVE2.0，以便杂志可以根据需求采纳适合的清单。
- ARRIVE支持方。这部分包括杂志、资助方、机构和其他组织如何能够使用和推广本指南的相关信息。
- 本指南有多种语言版本。这将增进国际上对本指南的应用。

在哪里可以找到本指南

Percie du Sert N, Hurst V, Ahluwalia A *et al.* (2020). The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. *PLOS Biology*. doi: 10.1371/journal.pbio.3000410

Percie du Sert N, Ahluwalia A, Alam S *et al.* (2020). Reporting animal research: Explanation and Elaboration for the ARRIVE guidelines 2.0. *PLOS Biology*. doi: 10.1371/journal.pbio.3000411

致谢

我们向在本指南研发过程中参与德尔菲调查的专家组成员，以及在实地测试中付出时间和给予反馈的参与者们致谢。我们还要向中国EQUATOR中心的卞兆祥教授和段玉婷博士、诺和诺德中国研发中心的白玉博士对本指南的翻译表示感谢。

更多的信息

www.ARRIVEguidelines.org
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ARRIVE关键10条

这些条目是一篇稿件需要包含的、基本的、最小信息集合。如果没有这些信息，读者和同行评议将无法评估研究结果的可靠性。

研究设计	1	对于每个实验，给出简要的研究设计细节，包括： a. 比较的组别，包括对照组。如果没有对照组，应阐明理由。 b. 实验单元（如以单只动物、一窝动物或一笼动物为单元）。
样本量	2	a. 详细说明分配给每个实验组的确切实验单元，以及每次实验的动物总数，整个实验使用的动物总数也需要说明。 b. 解释样本量是如何决定的。如已计算样本量，提供任何预先计算的细节。
纳入和排除标准	3	a. 描述实验期间用于纳入和排除动物(或实验单元)的任何标准，以及分析过程中的数据点。详细说明纳入和排除标准是否是预先设立的。如果没有设立相关标准，则给予明确的声明。 b. 对于每个实验组，报告分析中排除的动物、实验单元或数据点，并说明原因。如果没有排除动物的情况，请说明。 c. 对于每次分析，报告每个实验组中实验单元的准确数量。
随机化	4	a. 说明是否采用随机化方法将实验单元分配给对照组和处理组。如已随机化分配，提供产生随机化序列的方法。 b. 描述用于最小化潜在混杂因素的策略，如处理和测量的顺序，或者动物/笼子的位置。如果没有控制混杂因素，则给予明确的声明。
盲法	5	描述谁会在实验的不同阶段（分配、实验实施、结局评估、数据分析）知晓分组情况。
结局评价	6	a. 清晰地定义所有评估结局的措施（如细胞死亡、分子标记、或行为改变）。 b. 对于测试假说的研究，明确主要结局测量方法，如用于确定样本量的结局测量。
统计方法	7	a. 提供用于每次分析的统计方法的细节，包括使用的软件。 b. 描述用于评估数据是否能满足统计假设的任何方法，以及当统计假设无法满足时所做的方法变更。
实验动物	8	a. 提供使用动物种类的详细资料，包括物种、品系、亚系、雌雄、年龄或发育阶段，以及重量（如果相关的话）。 b. 提供进一步的相关信息，如动物来源、健康/免疫状态、基因修饰状态、基因型和任何先前的实验使用情况等。
实验步骤	9	对于每个实验组（包括对照组），描述可让其他研究人员重复的、足够的实验细节，包括： a. 内容（做了什么）、方法（怎么做的）、材料（用了什么）。 b. 时间和频次。 c. 地点（包括任何适应期的细节）。 d. 原因（提供进行这些程序的理由）。
结果	10	对于每次实验，包括独立重复的过程，报告： a. 对于每个实验组的总结/描述性统计，如果适用，应报告结局指标的变异度(如均值和标准差、或中位数和范围)。 b. 如果适用，应报告效应量及其可信区间。

建议条目集

这部分条目与“关键10条”互为补充，以增加研究的重要背景内容。两部分条目内容都报告是最佳的。

摘要	11	提供一个准确的、有关研究目标、动物物种、品系和雌雄、关键方法、主要结果和研究结论的摘要。
研究背景	12	a. 包括足够科学背景，有助理解研究的理由和背景内容，并解释实验方案。 b. 解释实验中使用的动物种类和模型如何达到研究目标，如果适用时，请解释与人类生物学的相关性。
研究目标	13	清楚地描述研究问题、研究目标，如果适用时，研究的具体假说。
伦理声明	14	提供批准本次使用动物进行实验研究的伦理审查委员会或相应机构的名称，以及任何相关许可证或方案编号(如适用)。如果没有寻求或未得到伦理批准，则需说明原因。
饲养场所和饲养	15	提供饲养场所和饲养条件的细节，包括任何环境方面的改善措施的内容。
动物饲养、监测	16	a. 描述在实验方案中为减轻动物疼痛、折磨和苦痛而采取的任何干预措施或步骤。 b. 报告任何预期或非预期的不良事件。 c. 描述为研究建立的人道终点，被监测的指征和监测的频率。如果研究未采用人道终点，请予说明。
诠释/科学内涵	17	a. 结合研究目标和假设、目前的理论和其他相关的文献研究等，解释结果。 b. 评价研究的局限性，包括潜在的偏倚来源、动物模型的局限性和结果的不精确性。
可推广性/转化	18	评论这项研究的结果是否，以及如何有可能适用于其他物种或实验条件，包括任何与人类生物学的关联(适用时)。
实验方案注册	19	提供一份声明说明是否在研究前准备了实验方案(包括研究问题、关键设计特点和分析计划)，该实验方案是否进行了注册，以及在何处注册。
数据获取	20	提供一份声明描述研究数据是否可获取，以及何处可以获得。
利益冲突声明	21	a. 声明任何潜在的利益冲突，包括经济上的和非经济上的。如果不存在利益冲突，也应声明。 b. 列出所有的资助来源（包括课题识别号）以及资助方在研究设计、分析和报告中所起的作用。

ARRIVE指南2.0是一部更新的报告动物研究的指南。ARRIVE指南2.0于2020年7月在*PLOS Biology*杂志上首次发表。

ARRIVE

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

The ARRIVE guidelines 2.0

Animal Research: Reporting of *In Vivo* Experiments

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The ARRIVE guidelines 2.0 are a checklist of information to include in publications describing animal research, published in *PLOS Biology* in July 2020. They ensure that studies are reported in enough detail to add to the knowledge base. This transparency enables readers and reviewers to scrutinise the research adequately, evaluate its methodological rigour, and reproduce the methods or findings.

Improving transparency in animal research – why ARRIVE?

Issues around the reproducibility of research involving animals cause significant concern among scientists, funders, and policy makers.

Transparent and accurate reporting is a cornerstone of reproducibility. It allows the research to be assessed effectively so it can inform future research, policy, and clinical practice.

However, animal research publications often lack important information, which prevents adequate evaluation of the methods and findings. To address this, the ARRIVE guidelines were first published in 2010. The updated guidelines – ARRIVE 2.0 – were released in 2020, along with a separate Explanation and Elaboration document providing further context.

Introducing ARRIVE 2.0

ARRIVE 2.0 is the result of an extensive, international collaboration, with input from the scientific community carefully built into the process. The authors of the guidelines include funders, journal editors, methodologists, statisticians, and researchers from academia and industry. Additional input from external stakeholders was gathered via a Delphi exercise. The guidelines were also road-tested by researchers preparing manuscripts, to ensure that they are well-understood and useful in practice.

The guidelines are relevant to any study involving live animals, from mammals to fish, as well as invertebrates, in any area of the biosciences.

To allow for initial focus on the most critical issues, the items which make up the guidelines are classified into two prioritised sets, with no ranking within each set. Both are provided overleaf. Reporting the items in both sets represents best practice.

How to use the guidelines

The guidelines are useful to consult throughout the course of a study:

- **During study planning:** the guidelines and accompanying Explanation and Elaboration document provide recommendations on experimental design, minimisation of bias, sample size and statistical analyses, helping researchers design rigorous and reliable *in vivo* experiments.
- **During the conduct of a study:** this allows researchers to record important information about study methods, which will be needed later for manuscript preparation.
- **When writing a manuscript:** used as an *aide memoire* to ensure the manuscript contains all relevant information.
- **When reviewing a manuscript:** to ensure all relevant information is available to evaluate the research.

Resources to support the use of ARRIVE 2.0

A wide range of resources are available at www.ARRIVEguidelines.org. These include:

- **Explanation and Elaboration for each of the items in the guidelines.** This includes extensive advice on the design of animal experiments, provides the rationale and evidence behind each item in the guidelines, and gives clear examples of good reporting from the published literature.
- **Fillable ARRIVE 2.0 checklists.** This allows researchers to indicate the specific sections of a manuscript that contain information relating to each item. Checklists are available for the ARRIVE Essential 10 and for the full ARRIVE 2.0 so that journals can tailor their requirements.
- **ARRIVE supporters.** This includes information on how journals, funders, institutions and other organisations can use and promote the guidelines.
- **The guidelines are available in multiple languages.** This helps international uptake.

Where to find the guidelines

Percie du Sert N, Hurst V, Ahluwalia A *et al.* (2020). The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. *PLOS Biology.* doi: 10.1371/journal.pbio.3000410

Percie du Sert N, Ahluwalia A, Alam S *et al.* (2020). Reporting animal research: Explanation and Elaboration for the ARRIVE guidelines 2.0. *PLOS Biology.* doi: 10.1371/journal.pbio.3000411

Acknowledgements

We are grateful to the members of the expert panel who took part in the Delphi exercise during the development of these guidelines, and the participants in the road testing for their time and feedback.

Further information

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The ARRIVE Essential 10

These items are the basic minimum to include in a manuscript. Without this information, readers and reviewers cannot assess the reliability of the findings.

Study design	1	For each experiment, provide brief details of study design including: a. The groups being compared, including control groups. If no control group has been used, the rationale should be stated. b. The experimental unit (e.g. a single animal, litter, or cage of animals).
Sample size	2	a. Specify the exact number of experimental units allocated to each group, and the total number in each experiment. Also indicate the total number of animals used. b. Explain how the sample size was decided. Provide details of any *a priori* sample size calculation, if done.
Inclusion and exclusion criteria	3	a. Describe any criteria used for including and excluding animals (or experimental units) during the experiment, and data points during the analysis. Specify if these criteria were established *a priori*. If no criteria were set, state this explicitly. b. For each experimental group, report any animals, experimental units or data points not included in the analysis and explain why. If there were no exclusions, state so. c. For each analysis, report the exact value of *n* in each experimental group.
Randomisation	4	a. State whether randomisation was used to allocate experimental units to control and treatment groups. If done, provide the method used to generate the randomisation sequence. b. Describe the strategy used to minimise potential confounders such as the order of treatments and measurements, or animal/cage location. If confounders were not controlled, state this explicitly.
Blinding	5	Describe who was aware of the group allocation at the different stages of the experiment (during the allocation, the conduct of the experiment, the outcome assessment, and the data analysis).
Outcome measures	6	a. Clearly define all outcome measures assessed (e.g. cell death, molecular markers, or behavioural changes). b. For hypothesis-testing studies, specify the primary outcome measure, i.e. the outcome measure that was used to determine the sample size.
Statistical methods	7	a. Provide details of the statistical methods used for each analysis, including software used. b. Describe any methods used to assess whether the data met the assumptions of the statistical approach, and what was done if the assumptions were not met.
Experimental animals	8	a. Provide species-appropriate details of the animals used, including species, strain and substrain, sex, age or developmental stage, and, if relevant, weight. b. Provide further relevant information on the provenance of animals, health/immune status, genetic modification status, genotype, and any previous procedures.
Experimental procedures	9	For each experimental group, including controls, describe the procedures in enough detail to allow others to replicate them, including: a. What was done, how it was done and what was used. b. When and how often. c. Where (including detail of any acclimatisation periods). d. Why (provide rationale for procedures).
Results	10	For each experiment conducted, including independent replications, report: a. Summary/descriptive statistics for each experimental group, with a measure of variability where applicable (e.g. mean and SD, or median and range). b. If applicable, the effect size with a confidence interval.

The Recommended Set

These items complement the Essential 10 and add important context to the study. Reporting the items in both sets represents best practice.

Abstract	11	Provide an accurate summary of the research objectives, animal species, strain and sex, key methods, principal findings, and study conclusions.
Background	12	a. Include sufficient scientific background to understand the rationale and context for the study, and explain the experimental approach. b. Explain how the animal species and model used address the scientific objectives and, where appropriate, the relevance to human biology.
Objectives	13	Clearly describe the research question, research objectives and, where appropriate, specific hypotheses being tested.
Ethical statement	14	Provide the name of the ethical review committee or equivalent that has approved the use of animals in this study, and any relevant licence or protocol numbers (if applicable). If ethical approval was not sought or granted, provide a justification.
Housing and husbandry	15	Provide details of housing and husbandry conditions, including any environmental enrichment.
Animal care and monitoring	16	a. Describe any interventions or steps taken in the experimental protocols to reduce pain, suffering and distress. b. Report any expected or unexpected adverse events. c. Describe the humane endpoints established for the study, the signs that were monitored and the frequency of monitoring. If the study did not have humane endpoints, state this.
Interpretation/ scientific implications	17	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 potential sources of bias, limitations of the animal model, and imprecision associated with the results.
Generalisability/ translation	18	Comment on whether, and how, the findings of this study are likely to generalise to other species or experimental conditions, including any relevance to human biology (where appropriate).
Protocol registration	19	Provide a statement indicating whether a protocol (including the research question, key design features, and analysis plan) was prepared before the study, and if and where this protocol was registered.
Data access	20	Provide a statement describing if and where study data are available.
Declaration of interests	21	a. Declare any potential conflicts of interest, including financial and non-financial. If none exist, this should be stated. b. List all funding sources (including grant identifier) and the role of the funder(s) in the design, analysis and reporting of the study.

The ARRIVE guidelines 2.0: updated guidelines for reporting animal research. Originally published in *PLOS Biology*, July 2020.

ARRIVE

The ARRIVE guidelines 2.0: author checklist

The ARRIVE Essential 10

These items are the basic minimum to include in a manuscript. Without this information, readers and reviewers cannot assess the reliability of the findings.

Item		Recommendation	Section/line number, or reason for not reporting
Study design	1	For each experiment, provide brief details of study design including: a. The groups being compared, including control groups. If no control group has been used, the rationale should be stated. b. The experimental unit (e.g. a single animal, litter, or cage of animals).	
Sample size	2	a. Specify the exact number of experimental units allocated to each group, and the total number in each experiment. Also indicate the total number of animals used. b. Explain how the sample size was decided. Provide details of any *a priori* sample size calculation, if done.	
Inclusion and exclusion criteria	3	a. Describe any criteria used for including and excluding animals (or experimental units) during the experiment, and data points during the analysis. Specify if these criteria were established *a priori.* If no criteria were set, state this explicitly. b. For each experimental group, report any animals, experimental units or data points not included in the analysis and explain why. If there were no exclusions, state so. c. For each analysis, report the exact value of *n* in each experimental group.	
Randomisation	4	a. State whether randomisation was used to allocate experimental units to control and treatment groups. If done, provide the method used to generate the randomisation sequence. b. Describe the strategy used to minimise potential confounders such as the order of treatments and measurements, or animal/cage location. If confounders were not controlled, state this explicitly.	
Blinding	5	Describe who was aware of the group allocation at the different stages of the experiment (during the allocation, the conduct of the experiment, the outcome assessment, and the data analysis).	
Outcome measures	6	a. Clearly define all outcome measures assessed (e.g. cell death, molecular markers, or behavioural changes). b. For hypothesis-testing studies, specify the primary outcome measure, i.e. the outcome measure that was used to determine the sample size.	
Statistical methods	7	a. Provide details of the statistical methods used for each analysis, including software used. b. Describe any methods used to assess whether the data met the assumptions of the statistical approach, and what was done if the assumptions were not met.	
Experimental animals	8	a. Provide species-appropriate details of the animals used, including species, strain and substrain, sex, age or developmental stage, and, if relevant, weight. b. Provide further relevant information on the provenance of animals, health/immune status, genetic modification status, genotype, and any previous procedures.	
Experimental procedures	9	For each experimental group, including controls, describe the procedures in enough detail to allow others to replicate them, including: a. What was done, how it was done and what was used. b. When and how often. c. Where (including detail of any acclimatisation periods). d. Why (provide rationale for procedures).	
Results	10	For each experiment conducted, including independent replications, report: a. Summary/descriptive statistics for each experimental group, with a measure of variability where applicable (e.g. mean and SD, or median and range). b. If applicable, the effect size with a confidence interval.	

The Recommended Set

These items complement the Essential 10 and add important context to the study. Reporting the items in both sets represents best practice.

Item		Recommendation	Section/line number, or reason for not reporting
Abstract	11	Provide an accurate summary of the research objectives, animal species, strain and sex, key methods, principal findings, and study conclusions.	
Background	12	a. Include sufficient scientific background to understand the rationale and context for the study, and explain the experimental approach. b. Explain how the animal species and model used address the scientific objectives and, where appropriate, the relevance to human biology.	
Objectives	13	Clearly describe the research question, research objectives and, where appropriate, specific hypotheses being tested.	
Ethical statement	14	Provide the name of the ethical review committee or equivalent that has approved the use of animals in this study, and any relevant licence or protocol numbers (if applicable). If ethical approval was not sought or granted, provide a justification.	
Housing and husbandry	15	Provide details of housing and husbandry conditions, including any environmental enrichment.	
Animal care and monitoring	16	a. Describe any interventions or steps taken in the experimental protocols to reduce pain, suffering and distress. b. Report any expected or unexpected adverse events. c. Describe the humane endpoints established for the study, the signs that were monitored and the frequency of monitoring. If the study did not have humane endpoints, state this.	
Interpretation/ scientific implications	17	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 potential sources of bias, limitations of the animal model, and imprecision associated with the results.	
Generalisability/ translation	18	Comment on whether, and how, the findings of this study are likely to generalise to other species or experimental conditions, including any relevance to human biology (where appropriate).	
Protocol registration	19	Provide a statement indicating whether a protocol (including the research question, key design features, and analysis plan) was prepared before the study, and if and where this protocol was registered.	
Data access	20	Provide a statement describing if and where study data are available.	
Declaration of interests	21	a. Declare any potential conflicts of interest, including financial and non-financial. If none exist, this should be stated. b. List all funding sources (including grant identifier) and the role of the funder(s) in the design, analysis and reporting of the study.	

·思路与方法学· 附加参考资料

动物实验《ARRIVE 声明》报告国际规范及促进结果利用的建议与思考

张雅静 刘建平

摘要 国内外均有大量的动物实验研究结果发表,然而从动物实验结果有效地转换到临床试验还需要大量研究证据。动物实验研究的实施、报告、评估不充分是动物实验结果得不到有效利用的主要原因。2010 年国际上发表了动物实验结果报告规范,即《ARRIVE 声明》。该声明由 20 个条目组成,细化了其中 11 项。ARRIVE 声明提供了发表动物实验所需信息详细列表。实验研究人员、稿件评审专家与杂志编辑可从前期研究方案注册与是否按照 ARRIVE 声明报告来进行质量控制与判断。以动物实验结果为前提的临床试验开展前应对动物实验进行整体性的系统综述,评审专家亦可以从是否进行动物实验的系统综述作为启动临床试验的重要依据之一。

关键词 动物实验; ARRIVE 声明; 临床试验; 报告规范

ARRIVE Statement for Animal Experiments: Suggestions and Thinkings on How to Internationally Standardize and Promote Their Utilization

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ABSTRACT Although more and more preclinical studies of animal experiments have been published at home and abroad, there is still some improvements from animal experiments to clinical trials. Inadequate enforcement, reporting, and evaluation of animal experimental researches are main causes for ineffective use of their results. *ARRIVE* (Animals in Research: Reporting *in vivo* Experiments) has been issued in 2010. It consists of a checklist of 20 items, and 11 items are detailed. It provided detailed information that all scientific publications reporting research using animals should include. Researchers, editors, and reviewers can control and judge the quality of animal experiments from preclinical registration and whether they followed *ARRIVE Statement* or not. A systematic review of animal experiments should be performed before clinical trials based on results of animal experiments, which could be taken by reviewers as one of important evidence for initiating clinical trials.

KEYWORDS animal experiment; *ARRIVE Statement*; clinical trial; report specification

在医学研究领域,人们常用动物实验来阐明疾病的生理、病理以及检验新的治疗措施的效果。动物实验主要目的之一在于新疗法运用于临床病人前的安全性和有效性评估。然而,从动物实验的结果有效转换到临床试验的效率却很低。一篇关于动物实验自身重复率的研究显示,动物实验自身结果得不到重复的比例高达 51% ~89%[1]。动物实验研究的实施、报告、评估不充分是动物实验阳性结果运用于临床试验时有效性得不到复制的主要原因[2]。

1 动物实验研究的前期研究方案注册

目前动物实验的设计、注册、报告和公开透明性的提高逐渐受到足够的重视。从以往动物实验系统综述的结果显示,动物实验的研究存在较大的报告偏倚(较多的为发表偏倚和选择性报告偏倚)[3]。为了避免这些偏倚,实验方案的前期注册就显得尤为重要。在临床试验中,研究方案的前期注册大多具有强制性,但是在动物实验中则很少会有研究者进行前期方案注册。为方便动物实验研究者进行方案注册,动物实验前期注册方案平台(https://www.preclinicaltrials.eu/)已开启使用。Preclinical Trials

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是世界范围内进行临床前期动物实验研究方案在线登记网站。该网站记录包括实验期间为减少偏倚的措施等研究方案的主要特征,并保存为永久性记录。注册不限于国家和地域,适用于所有的动物实验研究。Preclinical Trials 旨在提供临床前动物实验研究方案的全面信息。注册需要在实验开始时进行,以便提高研究的透明度,有助于避免重复,并通过将完成的研究与方案中计划的内容进行比较来降低报告偏倚的风险。

动物实验注册前需用邮箱建立一个账号,填写注册人员所在单位、姓名和国家。邮件进行账号确认后即可进行方案注册。实验注册分为一般信息和实验设计两部分。共含有 32 项,其中必填 25 项(一般信息 7 项,实验设计信息 18 项)。一般信息含有研究题目、主要实验负责人姓名、邮箱、联系方式以及联系人在实验中负责的任务,实验研究中心详细信息,资金来源,目前实验进行的阶段,实验开始日期以及实验预期结束日期。实验设计部分包含实验相关的领域、主要研究问题、实验干预措施类型、实验阶段类型(例如:阶段 1:基础机制研究,阶段 2:假设建立的探索性研究,阶段 3:最后确认性研究),还包括实验假设、主要结局指标及其测量时间与测量方法、动物以及组织是否只用于此实验、实验动物的品种、性别、实验动物模型、样本量计算方法、实验预计最后统计分析的样本数量,以及各实验组及其目的、随机分组方法、盲法、是否使用安慰剂对照、是否开展预实验、随访时长等信息。注册时可提供原始伦理批件或伦理批件号码。

2　动物实验报告规范——《ARRIVE 声明》

由于动物模型造价昂贵,资源的充分利用显得尤为重要。有研究表明,临床试验中试验过程报告不充分会影响临床试验结果的采用,从而导致大量科研及医疗资源的浪费[4]。正如临床试验研究一样,完整的报告有利于动物实验结果的应用。继 CONSORT 声明(随机对照试验的报告规范)广泛应用后,许多报告规范也相应发表。2010 年由牛津大学统计学家 Altman 教授,英国伦敦实验动物替代、减少、优化研究中心 Kilkenny 教授,英国布里斯托兽医学院 Browne 教授,英国布里斯托生物科学院 Cuthill 教授,帝国理工学院国家心肺研究中心 Emerson 教授起草。召集多学科(科学家、统计学家、杂志编辑以及研究者)组成专家小组通过会议讨论共同达成共识,同意以 CONSORT 为基础的关于动物实验的报告规范 ARRIVE 声明——《Animals in Research: Reporting *In Vivo* Experiment》的进一步推广与实施。该声明由英国伦敦实验动物替代、减少、优化研究中心以及医学研究委员会,生物技术与生物科学研究委员会,威康信托基金会,英国皇家学会,医学研究慈善协会,英国心脏基金会,帕金森病学会提供基金支持[5]。

《ARRIVE 声明》由 20 个条目组成(见表 1),包括了所有动物实验发表的重要信息。细化了其中 11 项。其中描述了所有研究类杂志使用动物进行研究必须报告的最少信息,如使用动物的数量和具体特征(包括物种或菌株类型、性别和遗传背景);饲养环境及饲养的详情;以及实验、统计和分析方法(包括用于减少偏倚的方法细节,如随机和盲法)。《ARRIVE 声明》可适用于任何使用实验动物的生物科学研究领域,其内在原则不仅适用于报告比较性的实验,也适用于其他研究设计(见表 1)。

3　研究质量评估与控制

学术期刊应将实验是否进行前期注册作为是否发表的条件之一。同时学术期刊在递交稿件给杂志编辑人员以及审稿专家时,应提供相关工具帮助他们判断有无选择性报告偏倚与实验结果后假设的问题。《ARRIVE 声明》既可以为研究者提供了一份清单,用来指导研究者准备投稿刊登的研究,也可以作为期刊文章同行评审专家的一份完整、透明的清单来确保高质量动物实验研究的发表。随着高质量、可开放获取的研究结果出现,完整的方法学注册方案和结果数据的获得,除了实验研究需要进行前期注册,实验的资金投资方也应进行注册。对于没有及时公布最终方法和结果的实验研究,则应扣留未使用的基金。

4　动物实验研究文献系统综述的必要性

如何使动物实验能够成为临床试验最珍贵、最值得信任的前期实验研究? 动物实验的系统综述在显示当前动物实验的局限性与提示动物实验结果转换到临床试验,并对结果出现不一致的原因进行分析报告,进而提供了有用的证据支持[6]。例如,临床试验的启动往往是先有一个动物实验结果显示有效,但是最后临床试验结果往往会得出与动物实验结果不同的、无效甚至有害的结论。为了避免此类现象发生,在开展以动物实验结果为基础的临床试验前应进行一个全面的动物实验研究的系统综述。除此之外,类似于 Cochrane 协作组织在 1992 年为提高临床试验系统综述的报告规范,动物实验 CAMARADES(Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies)已成立协作网并开发 SyRF(http://syrf.org.uk/)平台来有效促进动物实验研究的系统综述实施与质量保证。

表 1　动物实验研究报告的 ARRIVE 声明

文章结构	条目	描述信息
标题	1	提供简明、精确的研究内容描述
摘要	2	提供该研究简介的背景介绍,研究目的(阐述具体适用的动物品种),主要研究方法,主要研究结果,结论
引言		
背景	3	3[a]充分的科学背景(包括前期工作的相关文献)来阐述研究目的与研究原因,解释实验的方法与基本原理 3[b]为什么以及怎样使用该动物种类与模型可以解释科学目的
目的	4	特定的主要、次要研究目的或者具体的实验假说
方法		
伦理声明	5	指出研究涵盖的所有的伦理审查许可的性质、相关的许可证(例如,动物[科学程序]法案 1986)。表明国家或机构关于动物的护理和使用的制度指南
研究设计	6	每一个实验,给出简洁的实验设计细节:包括: 6[a]实验组与对照组实验数量 6[b]动物分配及结果计算时避免主观偏倚的方法(例如随机方法,何时何人进行盲法) 6[c]实验组(例如:单个动物,一组或者一笼动物) 给出相应时间图或流程图
干预措施	7	详细描述每组的干预措施,例如: 7[a]如何实施[如药物配方和剂量、地点和管理途径、麻醉和镇痛使用(包括监测)、外科手术、安乐死方法)。提供任何专业设备的详细资料,包括供应商] 7[b]实施时间(例如,一天的某个时间) 7[c]实施地点(例如,家笼,实验室,水迷宫) 7[d]实施原因(例如,选择特定麻醉的理由,用药的途径,用药剂量)
实验动物	8	8[a]提供具体的动物型号,包括品种,血型,性别,生长阶段(例如:年龄的平均数,或者年龄的均数加减标准差),体重(例如:体重的平均数,或者体重的均数加减标准差) 8[b]提供进一步的相关信息,如动物来源、国际菌株命名法、遗传修饰状态(例如,基因敲除或转基因),基因型,健康/免疫状态,该动物原来是否接受过其他药物或实验等
饲养环境和饲养条件	9	细节提供: 9[a]饲养环境[如设施类型,如有无特异病原体(SPF)];笼型或饲养物种所需居住类型;垫底材料;笼子里的同伴;鱼缸形状和材料等 9[b]饲养条件(如养殖计划、光/暗循环、温度、用于鱼类的水质等、食品种类、获得食物和水的方法、环境强化) 9[c]在实验之前、期间或之后进行与福利相关的评估和干预
样本量	10	10[a]明确指出各组样本量及实验总样本量 10[b]提供样本量决定方法以及样本量估算细节 10[c]必要的话,说明每个实验独立、重复的次数
实验动物分配	11	11[a] 详细说明动物是如何分配给实验组的,包括随机化或配对 11[b]描述不同实验组的动物被治疗和评估的顺序
结果	12	明确确定评估的主要和次要实验结果(如细胞死亡、分子标记、行为改变)
统计分析	13	13[a] 提供每个分析所用的统计方法的细节 13[b] 为每个数据集指定分析单元(例如,单个动物、动物组、单个神经元) 13[c] 描述用于评估数据是否符合统计方法假设的任何方法
结果		
基线资料	14	对于每个实验组,在测试之前或进行治疗时,报告动物的相关特征和健康状况(例如体重、微生物状况和实验动物之前是否接受过其他药物或实验) 此信息可以制成表格陈述
数据分析	15	15[a]报告每个分析中每组动物的数量。报告绝对数字(例如,10/20,而不是 50%) 15[b]如果在分析中没有包含任何动物或数据需说明原因
结局和效应值	16	对每一项分析的结果进行报告,并测量精度(例如,标准误差或置信区间)
不良事件	17	17[a]详细报告各组所有重要不良事件 17[b]报告任何以减少不良事件为目的,对预先制定研究方案的修改
讨论		
解释/科学影响	18	18[a]解释结果,考虑到研究的目标和假设,目前的理论,以及其他相关的文献研究 18[b]评论研究的局限性:包括任何潜在的偏倚来源,动物模型的任何局限性,以及与结果有关的不精确性 18[c]描述实验方法或发现对研究中动物使用的替代、改良或减少(3Rs)的任何影响
可推广性	19	实验结果是否以及怎样推广于包括人体生物在内的其他物种与系统
基金支持	20	列出所有资金来源(包括资金号)和资金赞助者在实验研究中具体工作分配任务

动物实验研究的系统综述应该成为一种普及性研究。相对于其发表的数量而言,系统综述本身的质量也十分重要。如何确保动物实验系统综述的质量? 为避免资源浪费,在进行系统综述前应在 SyRF Protocol Registry(http://syrf.org.uk/protocols/)和 Evidence-based Preclinical Medicine(https://onlinelibrary.wiley.com/journal/2054703)上进行检索查看自己的选题是否已被注册以及是否在 Systematic Review Library 网站(http://syrf.org.uk/library/)上发表过。如同临床研究的系统综述一样,研究开始前,动物实验研究的系统综述应在 SyRF(Systematic Review & Meta-analysis Facility)Protocol Registry(http://syrf.org.uk/protocols/)上进行研究方案的注册,注册信息应包括为什么以及如何进行系统评估。且应该包括研究问题、背景和将要使用的方法(检索策略、纳入标准、数据提取、质量评估、数据综合和统计分析计划);使用 CAMARADES[7] 列表或 SYRCLE RoB[8] 工具进行质量评估。根据 PRISMA[9] 条目撰写完整体例的系统综述报告[10]。

当临床试验前期的动物实验系统综述证据成为启动临床试验前至关重要的第一步时,伦理委员会应要求对所有所做的动物研究系统综述进行审查,包括(如果可能的话)根据 GRADE 等级原则对证据的确定性进行评估。美国食品药品监督管理局和欧洲药品管理局等监督管理机构也应该对支持许可证申请的临床前证据的稳健性提出更高的要求。由于临床前证据的综合是一个高度专业化的技术领域,外部评审专家应该对证据摘要的质量进行评估,并就其结果的解释向管理者提供决策建议。

为了解决上述问题,开展动物实验的想法和观点也需要进一步的提高与完善。一些有效、可重复并且可应用于临床的实验研究与开展这类研究的人员应得到社会的认可与鼓励。MVA85A 疫苗就是对之前的动物研究进行更深入的分析,使动物实验的结果应用于临床研究的案例[11]。

综上所述,动物实验质量的提高需要研究者、审稿专家、资金赞助机构以及编辑人员的共同努力。高质量动物实验的实施与报告将是动物实验结果与临床试验报告的效果进行有机统一的基础。医学科研在一定程度上意味着不断查询新的研究结果的过程。动物实验的系统综述将动物实验进行了一次系统性检索和评价。涉及文献的再次检索可以为动物实验的结果较好地运用到后续的临床试验中提供进一步的保障。

利益冲突:无

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