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Objective: The aim of this study was to use the Animals in Research: Reporting *In Vivo* Experiments (ARRIVE) guidelines to evaluate the quality of reporting of recent gastric cancer animal experiments. **Materials and Methods:** A literature search of studies was performed using the Chinese Biomedical Literature Database, Chinese Journal Full-text Database, Chinese Scientific Journal Full-text Database, and Wanfang Database from January 2010 to December 2012. We extracted data using pre-prepared Excel data-extraction forms. Reporting quality was evaluated based on the ARRIVE guidelines. **Results:** Of the 1816 studies that were identified by our search, 170 were subjected to quantitative analysis using the ARRIVE guidelines. The results of the evaluation based on the ARRIVE guidelines were that 132 studies (77.61%) provided an accurate and concise description of baseline conditions and clinical conditions. Only 2 (1.18%) papers provided relevant certificates of ethical review or institutional guidelines, and 2 (1.18%) papers provided an explanation of animal experiments requiring algorithms and formulas for sample size. Forty-seven (27.65%) studies described in detail how animals were assigned to each experimental group, including the randomization procedure, 2 (1.18%) reported whether blinding was used, and 15 (8.82%) evaluated the limitations of the study. **Conclusions:** The reporting quality of recent animal experiments of gastric cancer is inadequate. We should improve not only the quality of the methodology but also the reporting quality of the animal experiments.

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Abstract

Objective: The aim of this study was to use the Animals in Research: Reporting *In Vivo* Experiments (ARRIVE) guidelines to evaluate the quality of reporting of recent gastric cancer animal experiments.

Materials and Methods: A literature search of studies was performed using the Chinese Biomedical Literature Database, Chinese Journal Full-text Database, Chinese Scientific Journal Full-text Database, and Wanfang Database from January 2010 to December 2012. We extracted data using pre-prepared Excel data-extraction forms. Reporting quality was evaluated based on the ARRIVE guidelines.

Results: Of the 1816 studies that were identified by our search, 170 were subjected to quantitative analysis using the ARRIVE guidelines. The results of the evaluation based on the ARRIVE guidelines were that 132 studies (77.61%) provided an accurate and concise description of baseline conditions and clinical conditions. Only 2 (1.18%) papers provided relevant certificates of ethical review or institutional guidelines, and 2 (1.18%) papers provided an explanation of animal experiments requiring algorithms and formulas for sample size. Forty-seven (27.65%) studies described in detail how animals were assigned to each experimental group, including the randomization procedure, 2 (1.18%) reported whether blinding was used, and 15 (8.82%) evaluated the limitations of the study.

Conclusions: The reporting quality of recent animal experiments of gastric cancer is inadequate. We should improve not only the quality of the methodology but also the reporting quality of the animal experiments.

Keywords: Animal experiments; gastric cancer; ARRIVE guidelines.

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Introduction

Among all cancers, gastric cancer is one of a few that has high morbidity, and it ranks second only to lung cancer in terms of mortality worldwide (*Global et al.,2003*). In China, from 2004 to 2005, gastric cancer had the third highest mortality rate of the 10 main malignant neoplasms (*Mortality et al.,2012*).

Early diagnosis of gastric cancer is very important for enhancing survival and quality of life. However, most gastric cancer is diagnosed at an advanced stage (*Zheng et al., 2015*). In preclinical studies, animal experiments provide a significant reference for clinical research of GC. Clinical research demands improvements in the quality of preclinical research, and progress can be made if clinicians can find ways to improve communication with animal researchers, whose pre-clinical work they may rely on (*Perel et al., 2007*). In addition, developing an appropriate animal model and scientific methodology are keys to optimizing the value of gastric cancer research.

An increasing number of papers involving animal experiments of gastric cancer have been published in biomedical journals. However, the reporting information remains insufficient in many publications (*Berglundh et al., 2012*). A recent study showed that only one in five studies use a blind outcome assessment, and only one in six controlled animal studies use randomization (*Macleod et al., 2010*). The scientific and practical value of many animal experiments cannot be maximized because of poor reporting quality. Furthermore, in systematic reviews of animal experiments, poor reporting quality makes it difficult for reviewers to accurately assess the quality of the methodologies of the included studies. The Animals in Research: Reporting *In Vivo* Experiments (ARRIVE) guidelines, which were based on the Consolidated Standards of Reporting Trials (CONSORT) statement (*Thoma et al.,2012; Schulz et al.,2010; Moher et al.,2001*), were funded and developed by the National Centre for the Replacement, Refinement, and Reduction of Animals in Research (NC3Rs) to improve reporting standards (*Baker et al.,2014*). The ARRIVE guidelines consist of a 20-item checklist evaluating six parts of a report, including the “Title”, “Abstract”, “Introduction”, “Methods”, “Conclusions”, and “Discussion” sections. Evaluation of the content includes the number and specific characteristics of the animals used in the experiments (including species, strain, sex, and genetic background), the details of housing and husbandry, and the experimental, statistical, and analytical methods (including the use of randomization and blinding to reduce bias). The ARRIVE guidelines are applicable not only for reporting but also for designing animal experiments.

Therefore, the aim of our study was to conduct a systematic review based on the ARRIVE guidelines for the reporting of data in animal experiments on gastric cancer and to analyse the reporting quality of gastric cancer in Chinese journals.

Materials and Methods

Inclusion and Exclusion Criteria

We included all animal experiments in gastric cancer that were published in Chinese journals between January 2010 and December 2012. Participants: mice, rats, and nude mice with gastric cancer; no humans; Intervention: no limitations; Comparisons: no limitations; Outcomes: no limitations; Study design: animal experiments. We excluded animal experiments that focused on induced tumours rather than primary tumours, those without specific interventions, those without comparison groups, and those conducted *in vitro*.

Database Search for Published Studies

We searched the published animal experiments in gastric cancer from January 2010 to December 2012 in the Chinese Biomedical Literature Database (CBM), the Chinese Journal Full-text Database (CJFD), the Chinese Scientific Journal Full-text Database (CSJD), and the Wanfang Database. The main search terms were as follows: “mouse”, “rat”, “nude mouse”, “animal experiments”, “*vivo* experiments”, and “basic research”. We used Endnote X4(http://www.down12.com/soft/2066.html) to manage the search results. The search strategy is presented in Appendix Text S1.

Selection of Studies

The search results were independently selected by two reviewers (Feng Yuchen and Zhang Lili). First, titles and abstracts were selected from a list based on the inclusion and exclusion criteria. Second, the full texts of the studies were reviewed based on the same criteria. Discrepancies were resolved through discussion (with Liu Yali).

Data Extraction and Evaluation of Quality

We predesigned a unified data-extraction form consisting of basic information (published journals and date, research institutions, first author) and information about reporting quality based on the ARRIVE guidelines (title, abstract, introduction, methods, results, and conclusions.) The ARRIVE guidelines consist of 39 sub-items in six sections evaluating the minimum information that all reporting of animal experiments should include (*Kilkenny et al.,2010*). We added an item to the checklist’s 11th sub-item (marked as 6f) to address whether the experiment designer applied blinding in the experimental process. Each item was assessed as ‘yes’ (if described in the animal experiment), or ‘no’ (if not described in the animal experiment). Thus, a total of 40 sub-items were assessed in our study. A point was given for each ‘yes’, for a total of 40 possible points. Extraction was performed independently by at least two reviewers. Disagreements concerning the suitability of an article were resolved by group discussions.

Data Processing and Statistical Methods

The ARRIVE score for each sub-item and its frequencies were calculated and expressed as the mean value ± standard deviation. The *t*-test was used for the review of subgroups. *P*-values less than 0.05 were considered statistically significant. Statistical analyses were performed using SPSS (version 20.0) and Microsoft Excel (version 2007) software.

Results

Search Results and Screening

The results of the search and screening procedure are shown in Figure 1. A total of 1816 studies were identified by the electronic search. After duplicate studies were removed, 1109 studies remained. We then read titles, abstracts, and full texts based on the inclusion and exclusion criteria. Ultimately, 170 studies met the inclusion criteria and were included in this study.

Basic Information

The characteristics of the included studies are shown in Table 1. Most of the studies (91.76%, 156/170) included a randomization of the subjects into groups. However, only 19 of the 156 (12.18%) studies described the method of randomization in detail (such as a random number table).

General Reporting Information

After assessing the included studies according to the ARRIVE guidelines, the results showed that the mean checklist score of studies published from 2010 to 2012 was 21.92 ± 3.01. However, there was no significant difference in the ARRIVE checklist score for studies published in 2010 and 2011 ($P > 0.05$) or for studies published in 2011 and 2012 ($P > 0.05$) (Table 2).

Reporting Information of "Methods"

Only 1.18% of all 170 included studies reported an ethical statement, such as the ethical review permission, relevant licenses, or national or institutional guidelines for animal care and use pertaining to the research. Concerning the study design, almost no studies used a time-line diagram or flow chart to illustrate how the study design was implemented. Of the 169 (99.41%) studies that reported information regarding drug formulations and doses, sites and routes of administration, anaesthesia and analgesia, surgical procedures, and methods of euthanasia, only 5.29% (9/170) provided an explanation of these aspects. We found that only 0.59% (9/170) of the included studies explained how the sample size was determined and provided details regarding any sample size calculation used. Full details describing how animals were assigned to experimental groups were reported by only 27.65% (47/170) of all included studies. Only 1.18% (2/170) of all included studies provided information regarding whether they used blinding to reduce bias. Concerning the quality of the statistical analysis, our results indicated that 20% (34/170) of all included studies provided details regarding statistical methods and described any methods used to assess whether the data met the assumptions of the statistical approach.

Reporting Information of "Methods"

Baseline data, such as each experimental group, relevant characteristics, and the health status of the animals (e.g., weight, microbiological status, and drug- or test-naive) prior to treatment or testing, were reported and tabulated in 10% (17/170) of all included studies. In 38.82% (66/170) of all included studies, the numbers were analysed, and missing animals or data were explained. Only 5.29% (9/170) of all included studies provided any information regarding adverse events.

Reporting Information of "Conclusions"

Comments about study limitations, including any potential sources of bias, any limitations of the animal model, and any imprecision associated with the results, were provided in 8.82% (15/170) of all included studies. All funding sources were listed, and the roles of the funders of the study were described in 55.88% (95/170) of all included studies.

Discussion

The ARRIVE guidelines were developed and funded by the NC3Rs to improve bioscience research reporting and the communication of research findings to the broader scientific community. However, our survey indicated that the reporting of recent gastric cancer animal research in China is not satisfactory. In particular, the "ethical statement", "statistical methods", and "experimental design" methods, such as randomization and blinding, were not sufficiently described. Some studies focusing on the reporting quality of animal experiments after 2010 in the area of periodontology, such as implant dentistry, have been assessed using the ARRIVE and modified ARRIVE guidelines (*Berglundh et al.,2012; Thoma et al.,2012; Schwarz et al.,2012; Vignoletti et al.,2012; Stadlinger et al.,2012*).

Missing experimental methods was the most serious problem identified in the recent animal experiment studies that were assessed. In particular, the ethical statement, sample size (especially regarding how the

number of animals was decided and the algorithm was chosen), randomization, and blinding were insufficiently described. We found that 95.88% (163/170) of all included studies provided details about the animals used, e.g., species, strain, sex, and weight. Thus, the reporting of basic animal information was satisfactory. Because these factors will potentially affect the experimental results (*Kilkenny et al.,2009*), authors should be obligated to report all basic information regarding the experimental animals. Concerning experimental sample size, the mean reporting rate was 95.29% (162/170). Reporting the number of animals is important so that the experimental results can be evaluated and the experiment can be repeated. Only 0.59% (1/170) of all included studies explained how the animal sample size was decided and provided the relevant algorithm or formula that was used. Explaining how the number of animals was decided improves experimental credibility. Providing a time-line diagram or flow chart allows readers to understand how the animal experiment was designed and carried out.

Randomization and blinding are good methods to reduce experimental bias. Randomization is essential because known or unknown sources of variation can lead to selective bias and influence experimental results. Formal randomization is a process used to allocate animals to experimental groups and is carried out to avoid any bias in assigning animals to treatment groups, making it more likely that the groups are truly comparable (*Kilkenny et al.,2009*). A recent study showed that failure to randomize is likely to result in an overestimation of the apparent treatment benefits of the interventions in animal trials (*Hirst et al.,2014*). In the assessment of experimental design, we found that the mean reporting rate of randomization was 91.76% (156/170). In other words, 156 of all included studies took steps, such as a randomization procedure, to minimize the effects of subjective bias when allocating animals to treatment groups. However, only 27.65% (47/170) of all included studies provided full details regarding how animals were assigned to experimental groups; the random number table was the most frequently used method. It is unclear which methods were used in the other studies that reported random allocation.

Experimenters are often influenced by many subjective elements when assessing results (*Festing et al.,2002*). Blinding is another measure used to reduce measure bias and improve the validity of experimental results when two or more treatments are being compared (*Festing et al.,2002*). Experiments that fail to employ blind outcome assessments exaggerate effect sizes in animal studies. However, only 1.18% of the 170 studies used blinding.

It is very important to completely report information regarding bias control, which is closely related to experimental scientific validity.

Only 20% of the 170 studies reported the methods used to assess whether the data met the assumptions of the statistical approach. Statistical analysis is important for biological experiments. A confidence interval (CI) is an index used to assess the general validity of the experimental results; a higher CI generally indicates a higher reliability of the experimental results. If the statistical methods are not described, it is difficult to judge the external validity of the experimental results.

Readers regard scientific publication as an important source of information. It is difficult for readers to fully access scientific information because of insufficiencies in reporting, which limits its application to future scientific research and policy development. Therefore, authors have a great responsibility to ensure that their scientific publications are comprehensive, accurate, and transparent. In the case of animal experiments, in particular, it is essential to provide adequate scientific background, ethical terms, and details regarding how the

animals are assigned to each experimental group.

There were some limitations in our study. Our research assessed animal experiments from only 2010 to 2012, and it was limited to gastric cancer. Our assessment process was not blinded. Our assessment criteria (yes or no) did not use partial information, such as a 0.5 score. Although we assessed reporting quality based on the ARRIVE guidelines, we failed to consider the weight of different items.

Conclusions

The results indicate that the reporting quality of animal experiments in gastric cancer in Chinese journals was inadequate and that much of the key information was missing, specifically concerning the experimental design, statistical analysis, and ethical terms. Therefore, the reporting quality of biomedical research needs immediate improvement. The ARRIVE guidelines should be used widely to improve the quality of animal experiments and experimental design, and they can also enhance the quality of systematic reviews of animal experiments.

Acknowledgements

We thank Wenbo Liu and Xiaokang Zhang (Lanzhou University) for previous contributions to this study.

ADDITIONAL INFORMATION AND DECLARATIONS

Funding

This study was supported by the National Natural Science Foundation of China (NCSF; grant number: 81101756), Foundation of Key Laboratory of Digestive System Tumors (grant number: lzujbky-2011-t03), Gansu Province; Fundamental Research Funds for the Central Universities.

Author Contributions

Yali Liu and Yumin Li conceived and designed the study. Yuchen Feng, Lili Zhang and Yali Liu searched the data. Yuchen Feng, Lili Zhang, Xiaohuan Feng, Qin Feng, Jingyi Luo, Zhaodi Bai, Haoyu Wu, Xin Tian and Yali Liu extracted the data and assessed the reporting quality of the animal experiments. Yuchen Feng and Yali Liu analysed the data. Yali Liu and Yumin Li interpreted the data. Yali Liu and Yuchen Feng participated in the writing the manuscript.

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Figure 1(on next page)

Figure 1

The result of the search and screening procedure

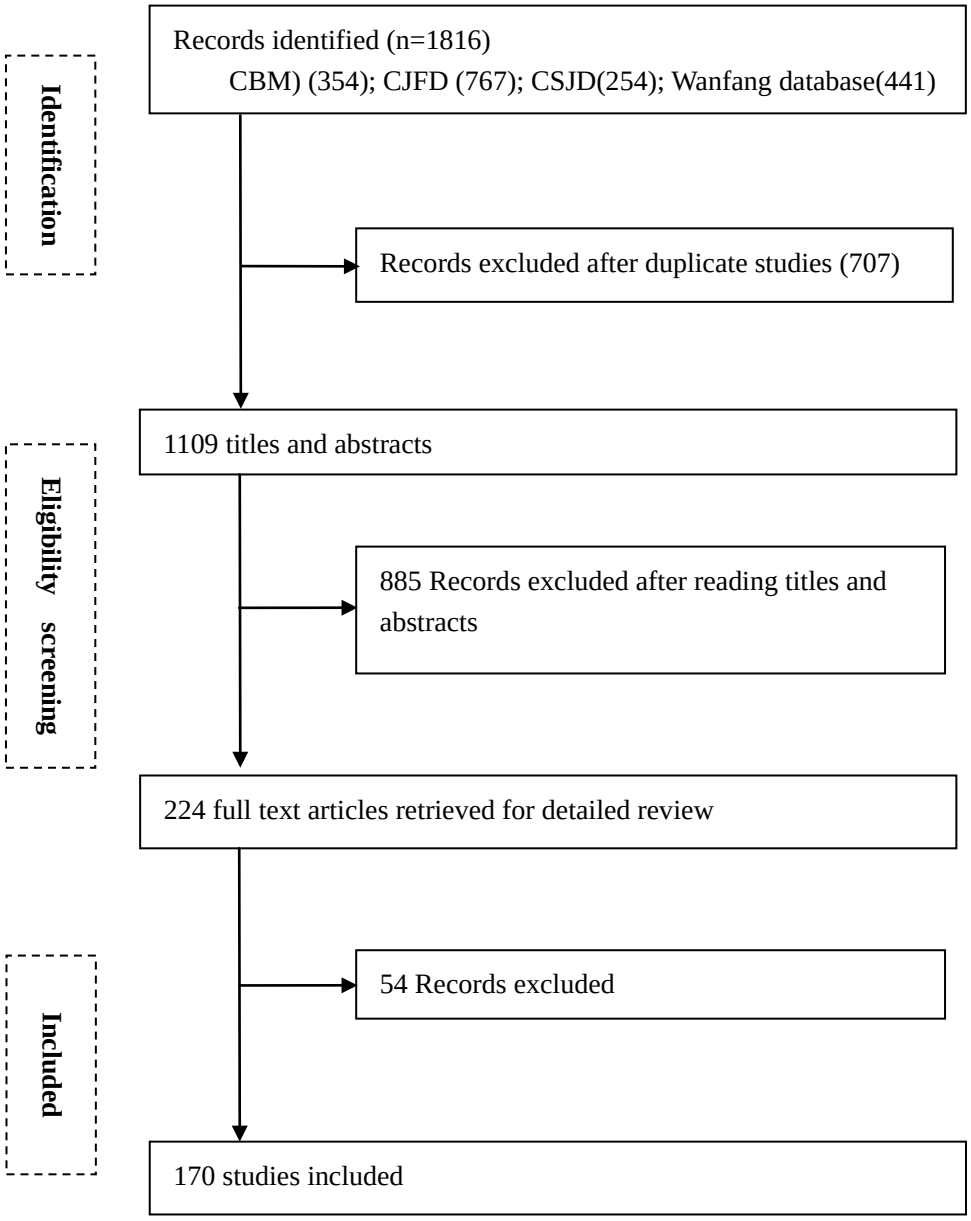

Figure 1. Flow chart for study selection

Table 1(on next page)

Table 1

The characteristics of the included studies

1 **Table 1. Characteristics of included studies**

Basic information		2010 number(%)	2011 number (%)	2012 number (%)	Sum number (%)
Included studies		69	59	42	170
RCTs		63(91.30)	55(93.22)	38(83.33)	156(91.76)
Type of cancers			Gastric cancer		
Numbers of Funding		46 (66.67)	28(47.48)	20(47.62)	94(55.29)
	0	23 (33.33)	31(52.54)	22(52.38)	76(44.71)
	1	41 (59.42)	16(27.12)	12(28.57)	69(40.59)
	2	4 (5.80)	3(5.08)	8(19.05)	15 (8.82)
	3	1 (1.45)	9(15.25)	0(0.00)	10(5.89)

2

Table 2(on next page)

Table 2

General Reporting Information

1 **Table 2 Reporting of checklists for ARRIVE Guidelines**

Item	Sub-item	Number	Recommendation	Sum number (%) n=170	2010 number (%) n=69	2011 number (%) n=59	2012 number (%) n=42
TITLE		1	Provide as accurate and concise a description of the content of the article as possible	161 (94.71)	63 （91.30）	57 （96.61）	41 （97.62）
ABSTRACT		2	Provide as 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	165 （97.06）	66 （95.65）	58 （98.31）	41 （97.62）
INTRODUCTION							
	Background	3a	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.	164 （96.47）	66 （95.65）	58 （98.31）	40 （95.24）
		3b	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	4（2.35）	3（4.35）	1（1.69）	0（0.00）

	Objectives	4	Clearly describe the primary and any secondary objectives of the study, or specific hypotheses being tested	166（97.65）	68（98.55）	58（98.31）	40（95.24）
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.	2（1.18）	0（0.00）	2（3.39）	0（0.00）
	Study design		*For each experiment, give brief details of the study design including:*				
		6a	For each experiment, give brief details of the study design, including a. The number of experimental and control groups.	163（95.88）	66（95.65）	55（93.22）	42（100）
		6b	b; Any steps taken to minimize the effects of subjective bias when allocating animals to treatment (e.g. randomization procedure)	156（91.76）	64（92.75）	53（89.83）	39（92.86）
		6c	c. The experimental unit (e.g. a single animal, group, or cage of animals).	169(99.41)	68(98.55)	59(100)	42(100)
		6d	d. A time-line diagram or flow chart can be useful to be illustrate how complex study designs were carried out.	0(0.00)	0(0.00)	0(0.00)	0(0.00)
		6f	If done, describe who was blinded (for	2(1.18)	1(1.45)	1(1.69)	0(0.00)

		example, outcome assessors) and how				
Experimental procedures	7a	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 suoolier(s).	169(99.41)	68(98.55)	59(100.00)	42(100.00)
	7b	b. When(e.g., time of day)	166(97.65)	67(97.10)	57(96.61)	42(100.00)
	7c	c. Where(e.g., home cage, laboratory, water maze).	106(62.35)	48(69.57)	36(61.02)	22(52.38)
	7d	d. Why (e.g., rationale for choice of specific anaesthetic, route of administration, drug dose used).	9(5.29)	5(7.25)	3(5.08)	1(2.38)
Experimental animals	8a	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).	163(95.88)	69(100.00)	52(88.14)	42(100.00)
	8b	b. Provide further relevant information such as the source of animals, international strain nomenclature, genetic	159(93.53)	69(100.00)	51(86.44)	39(92.86)

		modification status(e.g., knock-out or transgenic), genotype, health/immune status, drug or test-naïve, previous procedures,etc.				
Housing and husbandry	9a	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).	114(67.06)	52(75.36)	38(64.41)	24(57.14)
	9b	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).	110(64.71)	51(73.91)	37(62.71)	22(52.38)
	9c	c. Welfare-related assessments and interventions that were carried out before, during, or after the experiment.	0(0.00)	0(0.00)	0(0.00)	0(0.00)
Sample size	10a	a. Specify the total number of animals used in each experiment and the number of animals in each experimental group.	162(95.29)	65(94.20)	55(93.22)	42(100.00)
	10b	b. Explain how the number of animals was decided. Provide details of any sample size calculation used.	1(0.59)	1(1.45)	0(0.00)	0(0.00)
	10c	c. Indicate the number of independent replications of each experiment, if relevant.	4(2.35)	1(1.45)	3(5.08)	0(0.00)

	Allocating animals to experimental groups	11a	a. Give full details of how animals were allocated to experimental groups, including randomization or matching if done.	47(27.65)	19(27.54)	18(30.51)	10(23.81)
		11b	b. Describe the order in which the animals in the different experimental groups were treated and assessed.	166(97.65)	68(98.55)	58(98.31)	40(95.24)
	Experimental outcomes	12	Clearly define the primary and secondary experimental outcomes assessed(e.g. ell death, molecular markers, behavioral changes).	168(98.82)	69(100.00)	58(98.31)	41(97.62)
	Statistical methods	13a	a. Provide details of the statistical methods used for each analysis.	157(92.35)	64(92.75)	55(93.22)	38(90.48)
		13b	b. Specify the unit of analysis for each dataset(e.g. single animal, single neuron).	133(78.24)	54(78.26)	44(74.58)	35(83.33)
		13c	c. Describe any methods used to assess whether the data met the assumptions of the statistical approach.	34(20.00)	13(18.84)	12(20.34)	9(21.43)
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).	17(10.00)	7(10.14)	7(11.86)	3(7.14)
	Numbers analysed	15a	a. Report the number of animals in each	66(38.82)	31(44.93)	17(28.81)	18(42.86)

			group included in each analysis. Report absolute numbers (e.g. 10/20, not 50%)				
		15b	b. If any animals or data were not included in the analysis, explain why.	63(37.06)	28(40.58)	19(32.20)	16(38.10)
	Outcomes and estimation	16	Report the results for each analysis carried out, with a measure of precision (e.g. standard error or confidence interval).	157(92.35)	61(88.41)	54(91.53)	42(100.00)
	Adverse events	17a	a. Give details of all important adverse events in each experimental group.	9(5.29)	4(5.80)	2(3.39)	3(7.14)
		17b	b. Describe any modifications to the experimental protocols made to reduce adverse events.	1(0.59)	0(0.00)	1(1.69)	0(0.00)
DISCUSSION							
	Interpretation/scientific implications	18a	a. Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature.	167(98.24)	68(98.55)	58(98.31)	41(97.62)
		18b	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.	15(8.82)	8(11.59)	2(3.39)	5(11.90)
		18c	c. Describe any implications of your experimental methods or findings for the replacement, refinement or reduction (the	1(0.59)	1(1.45)	0(0.00)	0(0.00)

			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.	117(68.82)	49(71.01)	45(76.27)	23(54.76)
Funding		20	List all funding sources (including grant number) and the role of the funder(s) in the study.	95(55.88)	43 （62.32）	30(50.85)	22(52.38)

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