STROBE Statement—checklist of items that should be included in reports of observational studies

Section/item	Item No	Recommendation	Reported on Page Number/Line Number	Reported on Section/Paragraph
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	page 1,line 5-7	Title
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	page 2-3, line 51-89	Abstract
Introduction				
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	page 3-5, line 97-148	Introduction,Paragraph 1-2
Objectives	3	State specific objectives, including any prespecified hypotheses	page 5, line 149-161	Introduction,Paragraph 3
Methods				
Study design	4	Present key elements of study design early in the paper	None	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	page 6, line 176-184 page 8, line 253	Methods,Paragraph 2,9
Participants	6	(a) ***Cohort study***—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up ***Case-control study***—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls ***Cross-sectional study***—Give the eligibility criteria, and the sources and methods of selection of participants	page 6-7, line 185-232	Methods,Paragraph 3-7
		(b) ***Cohort study***—For matched studies, give matching criteria and number of exposed and unexposed ***Case-control study***—For matched studies, give matching criteria and the number of controls per case	page 7, line 208-232	Methods,Paragraph 5-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	page 8, line 235-249	Methods,Paragraph 8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	page 8, line 253-267	Methods,Paragraph 9-10
Bias	9	Describe any efforts to address potential sources of bias	None.	
Study size	10	Explain how the study size was arrived at	None.	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	None.	

Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	page 9-10, line 297-303	Methods,Paragraph 14
		(b) Describe any methods used to examine subgroups and interactions	None.	
		(c) Explain how missing data were addressed	None.	
		(d) ***Cohort study***—If applicable, explain how loss to follow-up was addressed ***Case-control study***—If applicable, explain how matching of cases and controls was addressed ***Cross-sectional study***—If applicable, describe analytical methods taking account of sampling strategy	None.	
		(e) Describe any sensitivity analyses	None.	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	page 10, line 297-303, 334-335;page 12, line	Results,Paragraph 1,4,6,7
		(b) Give reasons for non-participation at each stage	None.	
		(c) Consider use of a flow diagram	None.	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	page 10, line 309-314; page 11, line 336-339;	Results,Paragraph 1,4,6
		(b) Indicate number of participants with missing data for each variable of interest	page 10, line 309-310	Results,Paragraph 1
		(c) ***Cohort study***—Summarise follow-up time (eg, average and total amount)	None.	
Outcome data	15*	***Cohort study***—Report numbers of outcome events or summary measures over time	page 10, line 315-330;	Results,Paragraph 2-7
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	None.	
		(b) Report category boundaries when continuous variables were categorized	None.	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	None.	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	None.	
Discussion				
Key results	18	Summarise key results with reference to study objectives	page 14, line 442-449	Discussion,Paragraph 1
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	page 16, line 523-531	Discussion,Paragraph 7

Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	page 14-15, line 450-496	Discussion,Paragraph 2-5
Generalisability	21	Discuss the generalisability (external validity) of the study results	page 16-17, line 533-539	Conclusions,Paragraph 1
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	page 17, line 547-549	Acknowledgments

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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*As the checklist was provided upon initial submission, the page number/line number reported may be changed due to copy editing and may not be referable in the published version. In this case, the section/paragraph may be used as an alternative reference.

NOTE: Please save this file locally before filling in the table, DO NOT work on the file within your internet browser as changes will not be saved. Adobe Acrobat Reader (available free here) is recommended for completion.

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.	Methods,line 274-277
		b. The experimental unit (e.g. a single animal, litter, or cage of animals).	Methods,line 278
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.	Methods,line 278
		b. Explain how the sample size was decided. Provide details of any *a priori* sample size calculation, if done.	None.The sample size is determined according to references.
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.	Methods,line 287-288
		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.	there were no exclusions
		c. For each analysis, report the exact value of *n* in each experimental group.	Methods,line 278
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.	Methods,line 278-282
		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.	Confounders were not controlled
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).	N/A
Outcome measures	6	a. Clearly define all outcome measures assessed (e.g. cell death, molecular markers, or behavioural changes).	Methods,line 287-288
		b. For hypothesis-testing studies, specify the primary outcome measure, i.e. the outcome measure that was used to determine the sample size.	Methods,line 288-294
Statistical methods	7	a. Provide details of the statistical methods used for each analysis, including software used.	Methods,line 297-303
		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.	Methods,line 297-303
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.	Methods,line 270
		b. Provide further relevant information on the provenance of animals, health/immune status, genetic modification status, genotype, and any previous procedures.	Methods,line 270
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.	Methods,line 270-282
		b. When and how often.	Methods,line 282-286
		c. Where (including detail of any acclimatisation periods).	Methods,line 282-286
		d. Why (provide rationale for procedures).	Methods,line 270-273
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).	Results,line 407-430
		b. If applicable, the effect size with a confidence interval.	not applicable

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.	Abstract,line 79-81
Background	12	a. Include sufficient scientific background to understand the rationale and context for the study, and explain the experimental approach.	Introduction,line 121-148
		b. Explain how the animal species and model used address the scientific objectives and, where appropriate, the relevance to human biology.	not applicable
Objectives	13	Clearly describe the research question, research objectives and, where appropriate, specific hypotheses being tested.	Introduction,line 149-159
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.	Methods,line 291-294
Housing and husbandry	15	Provide details of housing and husbandry conditions, including any environmental enrichment.	All animals were reared adaptively for one wee
Animal care and monitoring	16	a. Describe any interventions or steps taken in the experimental protocols to reduce pain, suffering and distress.	None.
		b. Report any expected or unexpected adverse events.	None.
		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.	Methods,line 287-288
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.	Results,line 407-430
		b. Comment on the study limitations including potential sources of bias, limitations of the animal model, and imprecision associated with the results.	Discussion,line 523-531
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).	Discussion,line 497-520
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.	Methods,Page 9, line 292-295
Data access	20	Provide a statement describing if and where study data are available.	Data Sharing Statement
Declaration of interests	21	a. Declare any potential conflicts of interest, including financial and non-financial. If none exist, this should be stated.	Footnote,line 561
		b. List all funding sources (including grant identifier) and the role of the funder(s) in the design, analysis and reporting of the study.	Acknowledgments,line 547-548

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