

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	1/2	Title page
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3/38-58	Abstract/1-4
Introduction				
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6/65-93	Introduction/1-5
Objectives	3	State specific objectives, including any prespecified hypotheses	6/94-97	Introduction/5
Methods				
Study design	4	Present key elements of study design early in the paper	6/101-145	Methods/1-3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6/101-145	Methods/1-3
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	6/104-109	Methods/1
		(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	NA	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8/111-152	Methods/2-4
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	8/111-152	Methods/2-4
Bias	9	Describe any efforts to address potential sources of bias	NA	NA
Study size	10	Explain how the study size was arrived at	NA	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	NA	NA

Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8/148-154	Methods/4
		(b) Describe any methods used to examine subgroups and interactions	8/148-154	Methods/4
		(c) Explain how missing data were addressed	NA	NA
		(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	NA	NA
		(e) Describe any sensitivity analyses	NA	NA
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	9/169	Results/1
		(b) Give reasons for non-participation at each stage	NA	NA
		(c) Consider use of a flow diagram	NA	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1	Table 1
		(c) Cohort study —Summarise follow-up time (eg, average and total amount)	11/219-224	Results/4, Fig.5 and Table 1
Outcome data	15*	Cohort study —Report numbers of outcome events or summary measures over time	Table 1 and 2	Table 1 and 2
		Case-control study —Report numbers in each exposure category, or summary measures of exposure	NA	NA
		Cross-sectional study —Report numbers of outcome events or summary measures	NA	NA
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	9/170-171, 182-183, 217-224	Results/1,2, and 4
		(b) Report category boundaries when continuous variables were categorized	NA	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA	NA
Discussion				
Key results	18	Summarise key results with reference to study objectives	11-12/227-234	Discussion/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	15/306-320	Discussion/7

Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15/323-327	Conclusions/1
Generalisability	21	Discuss the generalisability (external validity) of the study results	15/323-327	Conclusions/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	15/330	Acknowledgements/1

*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 copyediting and may not be referable in the published version. In this case, the section/paragraph may be used as an alternative reference.

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: <ol style="list-style-type: none"> The groups being compared, including control groups. If no control group has been used, the rationale should be stated. The experimental unit (e.g. a single animal, litter, or cage of animals). 	
Sample size	2 <ol style="list-style-type: none"> 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. Explain how the sample size was decided. Provide details of any <i>a priori</i> sample size calculation, if done. 	
Inclusion and exclusion criteria	3 <ol style="list-style-type: none"> 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 <i>a priori</i>. If no criteria were set, state this explicitly. 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. For each analysis, report the exact value of <i>n</i> in each experimental group. 	
Randomisation	4 <ol style="list-style-type: none"> 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. 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 <ol style="list-style-type: none"> Clearly define all outcome measures assessed (e.g. cell death, molecular markers, or behavioural changes). 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 <ol style="list-style-type: none"> Provide details of the statistical methods used for each analysis, including software used. 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 <ol style="list-style-type: none"> Provide species-appropriate details of the animals used, including species, strain and substrain, sex, age or developmental stage, and, if relevant, weight. 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: <ol style="list-style-type: none"> What was done, how it was done and what was used. When and how often. Where (including detail of any acclimatisation periods). Why (provide rationale for procedures). 	
Results	10 For each experiment conducted, including independent replications, report: <ol style="list-style-type: none"> Summary/descriptive statistics for each experimental group, with a measure of variability where applicable (e.g. mean and SD, or median and range). 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.	