

Methods Reporting Checklist for Authors:

In accordance with the guidelines that emerged from a workshop led by the NIH, aimed at enhancing the scientific rigour and reproducibility of published results (accessed [here](#)), we have taken measures to ensure that we at [Future Science Group](#) are promoting good reporting standards. The checklist below is designed to establish if you have fulfilled the standards required by our journals.

Please check the below and indicate if the following information is available in your manuscript (or supplementary material). In cases where you have confirmed that the stipulated information is present in your article, please detail where it can be found by providing the page/paragraph/line number. If you feel that inclusion of this information is not applicable to your study, please indicate this in the column titled N/A.

For types of studies not covered by the methods checklist below, we recommend you consult the [Equator Network](#) website to identify a suitable guideline.

<u>General Methods</u>	Yes – information is located on page/paragraph/line:	N/A
1. I have detailed the exact sample size (<i>n</i>) for each experimental group/condition, as a number, not a range	Yes – information is located on page/paragraph/line: 4/2/1-14	
2. I have explained how sample size was chosen (in terms of having enough statistical power to make inferences about the sample)		N/A
3. For animal studies, I have included a statement about sample size estimate (NB. applicable even if no statistical methods were used)		N/A
4. A description of the sample collection is included, enabling the reader to understand whether the samples represent technical or biological replicates (including how many animals, litters, culture, etc.)	Yes – information is located on page/paragraph/line: 4/2/1-14	
5. I have defined how many times the experiment was replicated		N/A
6. I have detailed inclusion/exclusion criteria in cases where samples or animals were excluded from the analysis. I have detailed if the criteria were pre-established	Yes – information is located on page/paragraph/line: 2/2/1-8	

7. I have clarified the method of randomization that was used to determine how samples/animals were assigned to experimental groups		N/A
8. For animal studies: I have included a statement detailing whether or not randomization was used		N/A
9. For animal studies: I have included a statement detailing whether or not blinding was done		N/A
10. I have stated the extent to which the investigator was blinded to the group allocation during the experiment and/or when assessing the outcome		N/A

Statistical Testing

Yes – information is located on page/paragraph/line:

N/A

1. Statistical methods and measures have been defined: There is no need to describe very common tests, but more complex techniques should be described in the methods section. (For small sample sizes ($n < 5$) descriptive statistics are not appropriate, instead plot individual data points)	Yes – information is located on page/paragraph: 3/3 and 4/1	
2. I have stated if tests are one-sided or two-sided	Yes – information is located on page/paragraph/line: 4/1/14-15	
3. Statistical test results have been included e.g., <i>P</i> values	Yes – information is located on page/paragraph: 4/2-3 and 5/1-2	
4. 'Center values', such as median or mean have been defined	Yes – information is located on page/paragraph: 4/2-3	
5. Error bars (e.g., s.d. or s.e.m. or c.i.) have been defined	Yes – information is located on page/paragraph: 4/2-3	
6. I have stated if the data meet the assumptions of the tests (e.g., normal distribution)	Yes – information is located on page/paragraph: 3/1	

7. I have clarified if there is an estimate of variation within each group of data and, if so, I have detailed if the variance is similar between the groups that are being statistically compared

Yes – information is located on page/paragraph:
4/2-3

Reagents

**Yes – information is located on
page/paragraph/line:**

N/A

1. I have provided evidence that the antibodies were profiled for use in the system under study (assay and species), by giving a citation, catalog number and/or clone number, supplementary information or reference to an antibody validation profile (e.g., [Antibodypedia](#), [1DegreeBio](#))

N/A

2. I have clearly identified the source of cell lines and reported if they were recently authenticated (e.g., by STR profiling) and tested for mycoplasma contamination

N/A

Animal Models[†]

**Yes – information is located on
page/paragraph/line:**

N/A

1. I have reported the species, strain, weight, sex and age of animals

N/A

2. For experiments involving live vertebrates: I have either ticked to indicate that the necessary protocols have been followed in the Author Disclosure form or I have included a statement of compliance with ethical regulations and identified the committee(s) approving the experiments in my paper

N/A

[†] We recommend consulting the [ARRIVE guidelines](#) to ensure that other relevant aspects of animal studies are adequately reported.

Human Studies^{† ‡}
**Yes – information is located on
page/paragraph/line:**
N/A

1. I have identified the committee(s) approving the study protocol	Yes – information is located on page/paragraph/line: Title page/11/1-4	
2. I have included a statement confirming that informed consent was obtained from all subjects/ indicated that this is the case in the Author Disclosure form		N/A
3. I have reported the clinical trial registration number (at ClinicalTrials.gov or equivalent)		N/A

[†] For Phase II and III randomized controlled trials, we recommend that you refer to the [CONSORT statement](#).

[‡]For tumor marker prognostic studies, we recommend that you follow the [REMARK reporting guidelines](#).

Data and material sharing[†]
**Yes – information is located on
page/paragraph/line:**
N/A

1. I have stipulated in the manuscript that all datasets on which the conclusions of the report rely are available on request		N/A
2. I have provided accession codes for data that has been deposited in public repositories		N/A
3. If software has been used in the study: I have included information about the type of software and a statement describing if the software is available and how it may be obtained	Yes – information is located on page/paragraph/line: 4/1/14-15	

[†]We encourage the deposition of data to a discipline-specific, community-recognized repository where one exists, or a generalist repository if no suitable specific resource is available. Repositories can be found via sites such as re3data.org.

Health economic evaluations

Yes, see separate checklist:

N/A

1. I have followed the separate CHEERS[†] checklist, available [here](#).

N/A

† Husereau D, Drummond M, Petrou S *et al.*, on behalf of the CHEERS Task Force. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. *BMJ* 346, f1049 (2013).

Observational studies

Yes, see separate checklist:

N/A

1. I have followed the separate STROBE[†] checklist, available [here](#).

Yes, see separate checklist: STROBE_checklist

† von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *BMJ*. 335(7624), 806–808 (2007).

Systematic reviews & meta-analyses

Yes, see separate checklist:

N/A

1. I have followed the separate checklist established by [PRISMA](#)[†], available [here](#).

N/A

† Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 339, b2535 (2009).



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

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

	Item No	Recommendation
Title and abstract	1	<p>(a) Indicate the study's design with a commonly used term in the title or the abstract</p> <p>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</p>
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	<p>(a) <i>Cohort study</i>—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</p> <p><i>Case-control study</i>—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</p> <p><i>Cross-sectional study</i>—Give the eligibility criteria, and the sources and methods of selection of participants</p> <p>(b) <i>Cohort study</i>—For matched studies, give matching criteria and number of exposed and unexposed</p> <p><i>Case-control study</i>—For matched studies, give matching criteria and the number of controls per case</p>
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
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
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	<p>(a) Describe all statistical methods, including those used to control for confounding</p> <p>(b) Describe any methods used to examine subgroups and interactions</p> <p>(c) Explain how missing data were addressed</p> <p>(d) <i>Cohort study</i>—If applicable, explain how loss to follow-up was addressed</p> <p><i>Case-control study</i>—If applicable, explain how matching of cases and controls was addressed</p> <p><i>Cross-sectional study</i>—If applicable, describe analytical methods taking account of sampling strategy</p> <p>(e) Describe any sensitivity analyses</p>

Continued on next page

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
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure
		<i>Cross-sectional study</i> —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
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion

Key results	18	Summarise key results with reference to study objectives
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results

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
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*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.