2. Observational Study case

The following template, based on the STROBE statement (www.strobe-statement.org), can be used to critically appraise and evaluate the evidence in published papers reporting an observational study.

A. Title and abstract

1. Is the study design (i.e. cohort, case–control or cross-sectional study) clearly identified in the title?
2. Does the abstract provide a balanced summary of the study design, methods, results and conclusions as well as any major limitations?

B. Introduction

1. Is there a proper description of the scientific background and rationale for the current investigation? Has all the relevant information from any previous studies and other available evidence been included?
2. Is the primary objective of the current investigation indicated, and are secondary objectives described? Were all the objectives pre-specified? If a cohort study, were there any modifications to the original study protocol, including the formulation of additional objectives, following the publication of new evidence after the cohort study was initiated?

C. Methods

1. **Study design** Is the study design described adequately? In particular, is the type of study identified, and a description provided of the study setting and location as well as any relevant dates (including periods of recruitment, exposure, follow-up and data collection)?
2. **Participants**
   a) Are eligibility criteria (inclusion and exclusion) provided for the study participants? Are the sources and methods of selection of participants described?
   b) If a case–control study, is the rationale for the choice of cases and controls explained?
   c) If a cohort study, is the method of follow-up described?
   d) Was the study conducted using an appropriate spectrum of participants?
   e) If the study was matched, is information provided on the matching criteria and the number of exposed and unexposed participants (cohort study) or controls per case (case–control study)?
3. **Variables**
   a) Is there a clear description of outcomes, exposures, predictors, potential confounders and effect modifiers (with details of methods of assessment and diagnostic criteria, if applicable)?
   b) Are details provided on the comparability of assessment methods if there is more than one group?
4. **Bias** Have any efforts been made to address potential sources of bias? Are these fully described?
5. **Sample size** Is there a full explanation of how the study size was determined?
6. **Statistical methods**
   a) Is there a description of how numerical variables were handled in the analysis, including any choice of groupings?
   b) Are all the statistical methods used, including those adopted to control for confounding, fully described?
   c) If relevant, are the methods used to examine subgroups and interactions described?
   d) Is there a description of how missing data have been dealt with in all relevant analyses?
   e) Is there a description of how losses to follow-up (cohort studies), matching (case–control studies) or sampling strategy (cross-sectional studies) have been dealt with?
   f) Are all sensitivity analyses fully described?

D. Results

1. **Participant numbers and dates**
   a) Is there a report of the number of individuals included at each stage of the study (e.g. the numbers who are potentially eligible, are examined for eligibility, are confirmed eligible, are included in the study, completed follow-up and are included in the analysis), preferably through the use of a flow chart?
   b) If relevant, are reasons for nonparticipation at any stage documented?

2. **Descriptive data**
   a) Are the characteristics of study participants (demographic, clinical and social) and information on exposures and potential confounders provided?
   b) Is there an indication of the number of participants with missing data for each variable of interest?
   c) If a cohort study, is the follow-up time summarised (e.g. average and total amount)?
3. **Main results**
   a) *Main outcome measures.* Is there full information on outcomes, for example the number of outcome events or summary measures over time (cohort studies), numbers in each exposure category or summary measures of exposure (case–control studies) or number of outcome events or summary measures (cross-sectional studies)?
   b) *Magnitude of effects of interest.* Are unadjusted estimates and, if applicable, confounder-adjusted estimates provided?
   c) *Precision of effects of interest.* Is there an indication of the precision (e.g. 95% confidence intervals) of the estimates?
   d) If applicable, is there a clear indication of which confounders were adjusted for in the analysis and why they were selected?
4. **Other analyses** Are the results reported of all other analyses performed, including analyses of subgroups and interactions and any sensitivity analyses?

E. Discussion

1. **Summary of key results**
   a) Is there a summary of the key findings with reference to the study objectives?
   b) Do the results make **biological sense**?
   c) Consider the **confidence interval** for any effect of interest:
      (i) Would you regard the observed effect clinically important (irrespective of whether or not the result of the relevant hypothesis test is statistically significant) if the lower limit of the confidence interval represented the true value of the effect?
      (ii) Would you regard the observed effect clinically important if the upper limit of the confidence interval represented the true value of the effect?
      (iii) Are your answers to the above two points sufficiently similar to declare the results of the study unambiguous and important?
   d) If feasible, have any estimates of relative 'risk' (e.g. odds ratio or relative risk) been translated into absolute 'risks' for a meaningful time period?
2. **Limitations** Is there a discussion of all the study limitations, including the sources of imprecision and the sources and effect (i.e. direction and magnitude) of any potential bias?
3. **Generalisability** Is there a discussion of the generalisability (external validity) of the study findings (i.e. the extent to which the participants are representative of the wider population)?
4. **Interpretation** Are the study findings interpreted in a cautious way, taking full consideration of the study objectives, the limitations of the study, any multiple testing, the results from other similar studies and any other relevant evidence?

F. Other information

1. **Funding** Are the sources of funding documented both for the original study on which the article is based (if relevant) and for the present study, and is the role of the funders described?
2. **Conflict of interest** Is there a clear and transparent conflict-of-interest statement for each of the investigators?