## 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 | 3/58-66 | Abstract/1-6 |
| | | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | 4/78-79 | Conclusion/1-2 |
| **Introduction** | | | | |
| Background/ rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 5-6/91-110 | Introduction/2 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 5-6/91-110 | Introduction/2 |
| **Methods** | | | | |
| Study design | 4 | Present key elements of study design early in the paper | 6-7/115-133 | Patients and Methods/1 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6-7/115-133 and 7/150-159 | Patients and 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<br>***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<br>***Cross-sectional study***—Give the eligibility criteria, and the sources and methods of selection of participants | 6-7/115-133 and 7/150-159 | Patients and Methods/1,3 |
| | | (b) ***Cohort study***—For matched studies, give matching criteria and number of exposed and unexposed<br>***Case-control study***—For matched studies, give matching criteria and the number of controls per case | 6-7/115-133 and 7/150-159 | Patients and Methods/1,3 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 6-7/115-133 | Patients and Methods/2 |
| 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 | 8/150-159 | Patients and Methods(CTC Analysis)/5 |
| Bias | 9 | Describe any efforts to address potential sources of bias | 7/129-133 | Patients and Methods/2 |
| Study size | 10 | Explain how the study size was arrived at | 6/115-117 | Patients and Methods/1 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 8-9/150-159 | Patients and Methods(CTC Analysis)/5 |

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| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding | 8-9/162-177 | Patients and Methods |
| | | (b) Describe any methods used to examine subgroups and interactions | 8-9/162-177 | Patients and Methods |
| | | (c) Explain how missing data were addressed | 8-9/162-177 | Patients and Methods |
| | | (d) ***Cohort study***—If applicable, explain how loss to follow-up was addressed<br>***Case-control study***—If applicable, explain how matching of cases and controls was addressed<br>***Cross-sectional study***—If applicable, describe analytical methods taking account of sampling strategy | 8-9/162-177 | Patients and Methods (Statistical Analysis)/6 |
| | | (e) Describe any sensitivity analyses | 9/176-177 | Patients and Methods |
| **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 | 9/181-183 | Clinical Characteristics/1 |
| | | (b) Give reasons for non-participation at each stage | 9/181-182 | FigureS1 |
| | | (c) Consider use of a flow diagram | 9/181-182 | FigureS1 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 9/181-190 | Clinical Characteristics/1 |
| | | (b) Indicate number of participants with missing data for each variable of interest | 9/181-190 | Clinical Characteristics/1 |
| | | (c) ***Cohort study***—Summarise follow-up time (eg, average and total amount) | 9/181-190 | Clinical Characteristics/1 |
| Outcome data | 15* | ***Cohort study***—Report numbers of outcome events or summary measures over time | 9/181-190 | Clinical Characteristics/1 |
| | | ***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 | 10-11/204-217 | Survival Analysis in the matched cohorts;CTC |
| | | (b) Report category boundaries when continuous variables were categorized | 10-11/204-217 | Survival Analysis in the |
| | | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 10-11/204-217 | Survival Analysis in the |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 10-11/204-217 | Survival Analysis in the |
| **Discussion** | | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 11/220-230 | 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 | 14/288-298 | Discussion/5 |

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| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 13-14/267-283 | Discussion/2-4 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 13-14/267-283 | Discussion/4 |
| **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 | 15/306-313 | Funding Statement/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.