|  |  |  |  |
| --- | --- | --- | --- |
|  | Notes on Methodology Checklist 3: Cohort Studies | | |
| The studies covered by this checklist are designed to answer questions of the type “What are the effects of this exposure?”, It relates to studies that compare a group of people with a particular exposure with another group who either have not had the exposure, or have a different level of exposure. Cohort studies may be prospective (where the exposure is defined and subjects selected before outcomes occur), or retrospective (where exposure is assessed after the outcome is known, usually by the examination of medical records). | | | |
| **Section 1** | **Section 1** identifies the study, the reviewer, the guideline for which the paper is being considered as evidence, and the key question(s) it is expected to address. The reviewer is asked to consider a series of aspects of cohort study design and to make a judgement as to how well the current study meets this criterion. Each relates to an aspect of methodology that research has shown to be likely to influence the conclusions of a study.  Because of the potential complexity and subtleties of the design of this type of study, there are comparatively few criteria that automatically rule out use of a study as evidence. It is more a matter of increasing confidence in the strength of association between exposure and outcome by identifying how many aspects of good study design are present, and how well they have been tackled. A study that fails to address or report on more than one or two of the questions addressed below should almost certainly be rejected.  If you would like more information on cohort studies, their characteristics and weaknesses then please refer to Greenhalgh T. How to read a paper: the basics of evidence-based medicine. 3rd edition. Oxford: Blackwell;2006. Section 3.4 Page 49.  **Retrospective studies or single cohort studies are generally regarded as a weaker design, and should not receive a rating higher than “+”.**  Definitions for terms marked with a \* can be found in the [Cochrane Handbook](http://www.cochrane.org/glossary).  *{Note that the “Response” column is for guidance only. You may opt for a different rating depending on how information is presented in any given review.}* | | |
| **Statement 1.1** | **The study addresses an appropriate and clearly focused question** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | Unless a clear and well defined question is specified in the report of the review, it will be difficult to assess how well it has met its objectives or how relevant it is to the question you are trying to answer on the basis of the conclusions. | Always applies | **Yes -** if elements of the research question are present in the text.  **No** if there is no clear questioning the text.  **Can’t say -** if you think there is insufficient detail to allow an assessment to be made. |
| **Statement 1.2** | **The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | This relates to **selection bias**.\* It is important that the two groups selected for comparison are as similar as possible in all characteristics except for their exposure status, or the presence of specific prognostic factors or prognostic markers relevant to the study in question. | Only when there is a comparison group | **Yes** Where characteristics of the populations from which participants were selected are summarised (preferably in a table).  **No** Where there is no indication of how groups were selected, or what the relevant population characteristics were.  **Can’t say** Where source populations are identified, but no specific characteristics are tabulated.  **Not applicable** Where there is no comparison group. |
| **Statement 1.3** | **The study indicates how many of the people asked to take part did so, in each of the groups being studied.** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | This relates to **selection bias**.\* The participation rate is defined as the number of study participants divided by the number of eligible subjects, and should be calculated separately for each branch of the study. A large difference in participation rate between the two arms of the study indicates that a significant degree of **selection bias\*** may be present, and the study results should be treated with considerable caution. | Only in prospective, multiple cohort studies | **Yes** Where the participation rate per group is clearly defined.  **No** Where authors do not indicate the actual participation rate.  **Not applicable** Where there is no comparison group. |
| **Statement 1.4** | **The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis?** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | If some of the eligible subjects, particularly those in the unexposed group, already have the outcome at the start of the trial the final result will be subject to **performance bias.**\* A well conducted study will attempt to estimate the likelihood of this occurring, and take it into account in the analysis through the use of sensitivity studies or other methods. | Almost always applies | **Yes** Where sensitivity analyses are carried out to assess the impact of this occurring.  **No** Where no mention is made of this possibility.  **Can’t say** where the possibility is acknowledged, but no estimate of actual impact is made.  **not applicable** where the study relates to the long term effects of an existing condition. |
| **Statement 1.5** | **What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?** | | |
|  | ***What does this statement mean?*** | ***when does this statement apply?*** | ***Response:*** |
|  | This question relates to the risk of **attrition bias**.\*The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop out rate is regarded as acceptable, but in observational studies conducted over a lengthy period of time a higher drop out rate is to be expected. A decision on whether to downgrade or reject a study because of a high drop out rate is a matter of judgement based on the reasons why people dropped out, and whether drop out rates were comparable in the exposed and unexposed groups. Reporting of efforts to follow up participants that dropped out may be regarded as an indicator of a well conducted study. | In prospective studies | **Percentage** |
| **Statement 1.6** | **Comparison is made between full participants and those lost to follow-up, by exposure status.** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | For valid study results, it is essential that the study participants are truly representative of the source population. It is always possible that participants who dropped out of the study will differ in some significant way from those who remained part of the study throughout. A well conducted study will attempt to identify any such differences between full and partial participants in both the exposed and unexposed groups. This relates to the risk of **attrition bias**.\* Any unexplained differences should lead to the study results being treated with caution. | Prospective, multiple cohorts studies | **Yes** Where there has been some follow-up of drop outs, with explanation provided.  **No** Where there is no indication that this factor has been considered.  **Can’t say** Where dropout rates are mentioned, but no follow-up information is provided.  **not applicable** retrospective or single group studies. |
| **Statement 1.7** | **The outcomes are clearly defined** | | |
|  | ***What does this statement mean?*** | ***when does this statement apply?*** | ***Response:*** |
|  | This relates to the risk of **detection bias**.\* Once enrolled in the study, participants should be followed until specified end points or outcomes are reached. In a study of the effect of exercise on the death rates from heart disease in middle aged men, for example, participants might be followed up until death, or until reaching a predefined age. **If outcomes and the criteria used for measuring them are not clearly defined, the study should be rejected.** | Always applies | **Yes** Where endpoints or outcomes are clearly specified and used in the analysis.  **No** outcomes and measurement criteria are not discussed.  **Can’t say** Where definitions of outcomes and / or methods of measuring them are unclear. |
| **Statement 1.8** | **The assessment of outcome is made blind to exposure status** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | This relates to the risk of **detection bias.**\* If the assessor is blinded to which participants received the exposure, and which did not, the prospects of unbiased results are significantly increased. Studies in which this is done should be rated more highly than those where it is not done, or not done adequately. | In studies with more than one group | **Yes** Where assessors are blinded to exposure status.  **No** Where assessors could have been blinded, but were not.  **Can’t say -I**f randomisation is mentioned, but method not specified.  **not applicable** Where there is only one group being studied. |
| **Statement 1.9** | **Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | This relates to the risk of **detection bias.**\* Blinding is not possible in many cohort studies. In order to assess the extent of any bias that may be present, it may be helpful to compare process measures used on the participant groups - e.g. frequency of observations, who carried out the observations, the degree of detail and completeness of observations. If these process measures are comparable between the groups, the results may be regarded with more confidence. | Always applies | **Yes** Where process measures are detailed across groups, and are the same or similar for each.  **No** Where there is no indication if or how measures were managed.  **Can’t say** Where there is insufficient information to decide how comparable measures were across groups. |
| **Statement 1.10** | **The measure of assessment of exposure is reliable.** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | This relates to the risk of **detection bias.**\* A well conducted study should indicate how the degree of exposure or presence of prognostic factors or markers was assessed. Whatever measures are used must be sufficient to establish clearly that participants have or have not received the exposure under investigation and the extent of such exposure, or that they do or do not possess a particular prognostic marker or factor. Clearly described, reliable measures should increase the confidence in the quality of the study. | Always applies | **Yes** Where measures used are clearly defined and have a known degree of accuracy.  **No** Where measures are not defined.  **Can’t say** Where it is unclear which measures were used, or how they were defined. |
| **Statement 1.11** | **Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable.** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | This relates to the risk of **detection bias.**\* The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study. | Whenever any kind of subjective measure is used. | **Yes** Where clearly identified primary outcome measures are used in the analysis. If measures are subjective, justification for their use should be provided (eg validation of an assessment tool).  **No** Where outcome measures are not defined, or the analysis is based on secondary outcomes.  **Can’t say** Where subjective measures are described, but no indication given of how they were validated.  **not applicable.** Where measures used are completely objective. |

|  |  |  |  |
| --- | --- | --- | --- |
| **Statement 1.12** | **Exposure level or prognostic factor is assessed more than once** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | This relates to the risk of **detection bias.**\* Confidence in data quality should be increased if exposure level is measured more than once in the course of the study. Independent assessment by more than one investigator is preferable. | Prospective studies only. | **Yes** Where it is clearly stated that exposure level is measured more than once.  **No** Where it is clear that exposure was only checked once.  **Can’t say** Where there is no indication of when exposure was measured.  **not applicable** in retrospective studies. |
| **Statement 1.13** | **The main potential confounders are identified and taken into account adequately in the design and analysis** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | Confounding is the distortion of a link between exposure and outcome by another factor that is associated with both exposure and outcome. The possible presence of confounding factors is one of the principal reasons why observational studies are not more highly rated as a source of evidence. The report of the study should indicate which potential confounders have been considered, and how they have been assessed or allowed for in the analysis. Clinical judgement should be applied to consider whether all likely confounders have been considered. If the measures used to address confounding are considered inadequate, the study should be downgraded or rejected, depending on how serious the risk of confounding is considered to be. **A study that does not address the possibility of confounding should be rejected.** | Always applies | **Yes** Where the main potential confounders are discussed and sensitivity analyses carried out to see if and to what extent they may have affected results.  **No** Where there is no mention of confounding.  **Can’t say** Where confounding is mentioned, but no comment on or analysis of potential impact on results. |
| **Statement 1.14** | **Confidence intervals are provided** | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | Confidence limits are the preferred method for indicating the precision of statistical results, and can be used to differentiate between an inconclusive study and a study that shows no effect. Studies that report a single value with no assessment of precision should be treated with extreme caution. | Always applies | **Yes**  **No** |
| **Section 2** | **Section 2** relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on your responses in Section 1 and using the following coding system. The code allocated here, coupled with the study type, will decide the **level of evidence** that this study provides.  The aim of the other questions in this section is to summarise your view of the quality of this study and its applicability to the patient group targeted by the guideline you are working on. | | |

|  |  |
| --- | --- |
| **Statement 2.1** | **How well was the study done to minimise the risk of bias or confounding, and to establish a causal relationship between exposure and effect?** |

|  |  |  |
| --- | --- | --- |
|  | ++ | High quality (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. |
|  | + | Acceptable (+): Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. |
|  | 0 | Low quality (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies. |

|  |  |  |  |
| --- | --- | --- | --- |
| **Statement 2.2** | Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome? | | |
|  | ***What does this statement mean?*** | | |
|  | This is your clinical judgement of the study | | |
| **Statement 2.3** | Are the results of this study directly applicable to the patient group targeted in this guideline? | | |
|  | ***What does this statement mean?*** | ***When does this statement apply?*** | ***Response:*** |
|  | Does this study make sense in the Scottish context? | Always applies | **Yes**  **No** |
| **Statement 2.4** | **Notes.** Summarise the author’s conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This section is very important and will appear on the evidence table. **PLEASE FILL IN**. | | |
|  |  | | |