BMJ Open  Transcarotid versus transfemoral access for cerebrovascular intervention: protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction  Cerebrovascular intervention is an excellent option to treat cerebrovascular diseases. Interventional access is a prerequisite and a foundation for cerebrovascular intervention, which is crucial to the success of an intervention. Although transfemoral arterial access (TFA) has become a popular and acceptable method of access for cerebrovascular angiography and intervention in clinical practice, it has some drawbacks that limit the usage in cerebrovascular interventions. Therefore, transcarotid arterial access (TCA) has been developed in cerebrovascular interventions. We aim to conduct a systematic review to compare the safety and efficacy of TCA with TFA for cerebrovascular intervention.

Methods and analysis  In this protocol, Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols were followed. PubMed, Embase, Web of Science and the Cochrane Central Register of Controlled Trials will be searched mainly from 1 January 2004, to the formal search date. Additionally, reference lists and clinical trial registries will be searched. We will include clinical trials with more than 30 participants, which reported the endpoints of stroke, death and myocardial infarction. Two investigators will independently select studies, extract data and assess bias risk. A standardised mean difference with 95% CI will be presented for continuous data, and a risk ratio with 95% CI will be presented for dichotomous data. On inclusion of sufficient studies, subgroup analysis and sensitivity analysis will be conducted. The funnel plot and Egger’s test will be used to assess publication bias.

Ethics and dissemination  As only published sources will be used in this review, ethical approval is not required. We will publish the results in a peer-reviewed journal.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We will synthesise comprehensive evidence from more than 30 clinical trials in this systematic review and meta-analysis.
⇒ The Cochrane Collaboration criteria will be used to assess the risk of bias.
⇒ We will explore heterogeneity sources using subgroups and sensitivity analyses.

BACKGROUND

Cerebrovascular diseases, such as carotid artery stenosis, intracranial artery stenosis, aneurysms and malformations, cause severe long-term disability and death worldwide and negatively impact both public health and the economy.1 Cerebrovascular intervention is an excellent option to treat these diseases. In comparison to traditional open surgery, cerebrovascular intervention offers several advantages, including minimally invasive surgery, a wide range of indications, a shorter procedure time and reduced complications.2 With the advancement of continuous innovations in concepts, techniques and equipment, cerebrovascular intervention has become increasingly available in recent years.3 4

Interventional access is a prerequisite and a foundation for cerebrovascular intervention, which is crucial to the success of an intervention.5 Obtaining interventional access, therefore, is both critical and challenging. Transfemoral arterial access (TFA), introduced at the end of the 20th century for percutaneous coronary intervention, has become a popular and acceptable method of access for cerebrovascular angiography and intervention in clinical practice because it offers the advantages of being paid, technical simplicity, relatively painless and the ability to use larger catheters and equipment by clinicians.6 While TFA has been used with success for many years, it has some drawbacks including poor patient satisfaction, vascular complications, as well as some contraindications, such as peripheral vascular disease, femoral hernia and saddle embolism.7-12

Additionally, anatomic variants of the carotid artery or aortic arch prevent the
establishment of stable vascular access. Several factors have been identified as contributing to the difficulty of establishing TFA including aortic arch morphology that is unfavourable, extreme tortuosity of the common carotid artery, narrowing of the opening of the carotid artery and severe calcification of the aorta.\textsuperscript{15-17} As a result, transcarotid arterial access (TCA) has been developed to increase the safety and efficacy of cerebrovascular interventions.\textsuperscript{18} The procedure is accompanied by a dynamic flow reversal system that is designed to prevent embolism and perioperative embolic stroke in the patient.\textsuperscript{19, 20} Compared with TFA, TCA eliminates the need to traverse the aortic arch, reduces the production of debris and the risk of atheroembolisation, and takes a shorter procedure period.\textsuperscript{21} It has been shown in numerous clinical trials that TCA has a lower stroke rate.\textsuperscript{22-25} Despite this, the benefits and risks of TCA compared with TFA are unclear, and there is no guideline that assists clinicians in making the right choice. The purpose of this study is to compare the safety and efficacy of TCA versus TFA for cerebrovascular interventions.

Objective

We aim to assess the safety and efficacy of TCA compared with TFA in people undergoing cerebrovascular intervention. The primary outcome is the rates of composite endpoints within 30 days and 1 year. Composite endpoints include death, stroke and myocardial infarction (MI). The secondary outcomes include procedural times, length of hospital stay, total radiation dose, and the rates of death, stroke, MI, cranial nerve injury (CNI), transient ischaemic attack (TIA) and other local and systemic complications.

METHODS AND ANALYSIS

The Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) were followed during the development of this protocol (see online supplemental 1, PRISMA-P checklist). We have prospectively recorded this systematic review on the PROSPERO database (https://www.crd.york.ac.uk/PROSPERO/). We will promptly update on the PROSPERO registration if we do revisions to this protocol, and we will timely update the entire review process. We will conduct and report our systematic review following the Cochrane Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension statement.

Patients and public involvement

Neither patients nor members of the general public are involved in this study.

Criteria for considering studies for this review

Types of studies

We will include randomized controlled trials (RCTs), a means of testing the effectiveness of a therapy or drug in health care, quasi-RCTs and prospective or retrospective case-control studies comparing TCA with TFA with more than 30 participants of each arm. In vitro studies, animal research, case series, case reports, and registry studies will be excluded. We will also exclude duplicate publications. The study selection will be limited to English-language publications. No limit will be placed on publication status.

Types of participants

Adults (≥18 years old) undergoing cerebrovascular intervention for ischaemic and haemorrhagic cerebrovascular diseases. Ischaemic cerebrovascular diseases will be focused on cerebrovascular stenosis caused by atherosclerosis in extracranial and intracranial arteries. For example, adult patients with symptomatic or asymptomatic carotid artery stenosis (>50% for symptomatic and >70% for asymptomatic patients according to the North American Symptomatic Carotid Endarterectomy Trial criteria) will be included in the study.\textsuperscript{26} Haemorrhagic cerebrovascular diseases will be focused on intracranial artery aneurysms and malformations. There will be no gender restrictions.

Types of interventions

TCA for cerebrovascular intervention is the experimental intervention and TFA is the comparator. Cerebrovascular intervention includes mechanical thrombectomy, stenting, drug delivery, etc. Trials compared TCA with TFA for cerebrovascular intervention will be considered for the analysis.

Types of outcome measures

Inclusion will be restricted to studies reporting at least one of these outcomes.

Primary outcomes

1. The rates of composite endpoints within 30 days after surgery.
2. The rates of composite endpoints within 1 year after surgery.

Second outcomes

1. Procedural time.
2. Length of hospital stay.
3. Total radiation dose.
4. The rates of death, stroke, MI, CNI, TIA and other local and systemic complications within 30 days and 1 year after surgery.
5. The non-neurological complications such as bleeding at puncture site, subcutaneous haematoma and pseudoaneurysm.

Search methods for identification of studies

Searches will be conducted in PubMed, Embase, Web of Science and the Cochrane Central Register of Controlled Trials. Using the Peer Review of Electronic Search Strategies Checklist, an experienced librarian developed the search strategy for PubMed and another librarian revised it (see online supplemental 2, search strategy).
Additionally, grey literature, conference proceedings, WHO International Clinical Trials Registry Platform, ClinicalTrials.gov, and the reference and citation list of relevant published systematic reviews and included studies will also be searched for relevant studies. If additional information is needed, we will contact the corresponding authors. Only English-language studies published after 1 January 2004 will be included in the search. Publication status will not be restricted.

**Data extraction and analysis**

**Study selection**
A two-tiered screening and selection process will be conducted independently by two reviewers. At first, two reviewers will evaluate the searched studies based on their title and abstract, with the eligible studies advancing to a second level of screening. Subsequently, in level two screening, full texts of retained articles will be obtained and referred to screen articles meeting the eligibility criteria, and the retained studies will be included for follow-up analysis. It will be considered the study with the largest sample size or the most direct interventions when data from different publications come from the same study series or study population. If there are discrepancies, we will resolve them through discussion or involve a third reviewer. Furthermore, for each screening level, a pilot test will be conducted using predesigned test forms to determine inter-rater reliability, and 80% agreement is required for formal screening (see online supplemental 3, screening pilot-test form). When additional information is required, the corresponding authors will be contacted.

**Data extraction and management**
A predesigned data extraction form will be used by two independent reviewers to extract data from eligible studies. Discrepancies will be discussed or referred to a third reviewer. When clinical trials with multiple arms are included, only the appropriate arms with more than 30 participants will be included. We will extract the following information for every eligible study: trial name, authors, publication date, study design, intervention approach, number of patients, outcome data (follow-up period, rates of composite endpoints within 30 days and 1 year after surgery, procedural times, length of hospital stay, total radiation dose, and rates of death, stroke, MI, CNI, TIA and other local and systemic complications), procedural success rate (defined by trials), characteristics of participants (eg, median age, male to female ratio, specific diseases, baseline blood pressure, drinking and smoking status, medical history). The inter-rater reliability should also be calculated using a similar pilot test in order to confirm that two reviewers have achieved a high level of agreement (80%). Additional information will be sought from the corresponding author if needed.

**Assessment of risk of bias in included studies**
An assessment of bias risk in eligible RCTs will be conducted by two reviewers using the Cochrane Collaboration tool. The Newcastle-Ottawa Scale (see online supplemental 4, Newcastle-Ottawa Scale) will be applied to assess case-control studies. There will be a third investigator involved if there is any disagreement.

**Measure of treatment effect**
A mean difference will be used for continuous variables with 95% CIs for outcomes of the same scale, and a standardised mean difference will be used for outcomes of different scales. The risk ratio for dichotomous data will be calculated with a 95% CI.

**Dealing with missing data**
If necessary data or additional information are missing, the corresponding authors will be contacted. When missing data is not available, they will be imputed based on established methodologies, such as informative missingness difference of means when continuous outcomes are not available. Additionally, to ensure that our imputations do not affect the results, we will conduct a sensitivity analysis.

**Data synthesis and statistical analysis**

**Data synthesis**
When the data is insufficient or quantitative synthesis is not applicable, the findings will be reported narratively. A meta-analysis will be conducted whenever it is feasible to do a quantitative analysis with STATA (V.17, StataCorp, 2021). First, data from RCTs, then data from quasi-RCTs, and finally data from case-control studies will be included.

**Assessment of heterogeneity**
In order to determine whether methodological heterogeneity exists, the Q test will be applied to calculate the $I^2$ statistics. We will apply a random-effects model if the p value $<0.10$ or $I^2>50\%$, which indicates significant heterogeneity. Additionally, for identifying the source of heterogeneity, a subgroup analysis and sensitivity analysis will be conducted. The Mantel-Haenszel fixed-effect model is used to calculate the pooled estimates of safety and efficacy if p value $\geq0.10$ or $P\leq50\%$.

**Subgroup analysis and sensitivity analysis**
A subgroup analysis will be conducted if sufficient data are available for the purpose of exploring sources of heterogeneity, such as:
1. Gender (men and women).
2. Age (elderly vs young (80 years old as the cut-off)).
3. Types of diseases, such as acute stroke, subacute stroke versus chronic stroke; or ischaemic stroke versus haemorrhage stroke; or symptomatic versus asymptomatic carotid artery stenosis; or extracranial artery diseases versus intracranial artery diseases, if available. Acute stroke was defined as the course of a stroke within 14 days of onset, subacute stroke as the course of a stroke within 14–180 days of onset and chronic stroke as the course of a stroke after 180 days of onset.27
Our findings will be tested for robustness through sensitivity analyses. For meta-analysis, we will collect only data from RCTs, quasi-RCTs and case-control studies, and exclude each study individually. Then a comparison of the consistency of the results will be conducted.

Assessment of report bias
When there are 10 or more studies, a funnel plot analysis will be used to investigate publication bias. When the funnel plot exhibits asymmetry, Begg’s rank correlation and Egger’s weighted regression tests need to be performed.

Assessment of the certainty of the evidence
Evaluation of evidence’s quality will be performed using the Grading of Recommendation, Assessment, Development and Evaluation approach. There will be four levels of evidence strength: high, moderate, low or very low, depending on the risk of bias, consistency, directness, precision and publication bias. The results will be presented in the narrative form if a meta-analysis is not possible.

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Contributors
YK developed the initial idea for this study. JY and WL contributed to the original draft. DL and WX developed and revised the search strategy. ZW, RY, JW and HG will screen the potential studies independently, extract data from the included studies, assess the risk of bias and complete the data synthesis. YL, JG and CH will arbitrate in cases of disagreement and ensure the absence of publication bias. The funder of the study had no role in study design, data analysis, data interpretation and manuscript writing.

Competing interests
None declared.

Patient and public involvement
Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication
Not applicable.

Provenance and peer review
Not commissioned; externally peer reviewed.

Supplemental material
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REFERENCES


### PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

<table>
<thead>
<tr>
<th>Section and topic</th>
<th>Item No</th>
<th>Checklist item</th>
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<tbody>
<tr>
<td>ADMINISTRATIVE INFORMATION</td>
<td></td>
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<tr>
<td>Title:</td>
<td></td>
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</tr>
<tr>
<td>Identification</td>
<td>1a</td>
<td>Identify the report as a protocol of a systematic review Yes Page1, line 2</td>
</tr>
<tr>
<td>Update</td>
<td>1b</td>
<td>If the protocol is for an update of a previous systematic review, identify as such N/A</td>
</tr>
<tr>
<td>Registration</td>
<td>2</td>
<td>If registered, provide the name of the registry (such as PROSPERO) and registration number Yes Page3, line 69 Page5, line 149</td>
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<tr>
<td>Authors:</td>
<td></td>
<td></td>
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<tr>
<td>Contact</td>
<td>3a</td>
<td>Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author Yes Page1, line 7</td>
</tr>
<tr>
<td>Contributions</td>
<td>3b</td>
<td>Describe contributions of protocol authors and identify the guarantor of the review Yes Page11, line 298</td>
</tr>
<tr>
<td>Amendments</td>
<td>4</td>
<td>If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments Yes Page5, line 149</td>
</tr>
<tr>
<td>Support:</td>
<td></td>
<td></td>
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<tr>
<td>Sources</td>
<td>5a</td>
<td>Indicate sources of financial or other support for the review Yes Page10 line 291</td>
</tr>
<tr>
<td>Sponsor</td>
<td>5b</td>
<td>Provide name for the review funder and/or sponsor Yes Page10, line 292</td>
</tr>
<tr>
<td>Role of sponsor or funder</td>
<td>5c</td>
<td>Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol Yes Page11, line 294</td>
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<tr>
<td>INTRODUCTION</td>
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<td>Rationale</td>
<td>6</td>
<td>Describe the rationale for the review in the context of what is already known Yes Page4, line 97</td>
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<tr>
<td>Objectives</td>
<td>7</td>
<td>Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes Yes Page5, line 135</td>
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<tr>
<td>(PICO)</td>
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<tr>
<td><strong>METHODS</strong></td>
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<tr>
<td>Eligibility criteria</td>
<td>8</td>
<td>Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review</td>
</tr>
<tr>
<td>Information sources</td>
<td>9</td>
<td>Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage</td>
</tr>
<tr>
<td>Search strategy</td>
<td>10</td>
<td>Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated</td>
</tr>
</tbody>
</table>

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<tr>
<th>Study records:</th>
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<tbody>
<tr>
<td>Data management</td>
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<tr>
<td>Selection process</td>
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<tr>
<td>Data collection process</td>
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</tbody>
</table>

| Data items | 12 | List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications | Yes | Page 8, line 218 |

| Outcomes and prioritization | 13 | List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale | Yes | Page 6, line 173 |

| Risk of bias in individual studies | 14 | Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis | Yes | Page 10, line 269 |

<p>| Data synthesis | 15a | Describe criteria under which study data will be quantitatively synthesised | Yes | Page 9, line 248 |
| 15b | If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I², Kendall’s τ) | Yes | Page 8, line 233 |</p>
<table>
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<tr>
<td>15c</td>
<td>Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)</td>
<td>Yes</td>
<td>Page9, line 259</td>
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<tr>
<td>15d</td>
<td>If quantitative synthesis is not appropriate, describe the type of summary planned</td>
<td>Yes</td>
<td>Page9, line 247</td>
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<tr>
<td>Meta-bias(es)</td>
<td>16</td>
<td>Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)</td>
<td>Yes</td>
</tr>
<tr>
<td>Confidence in cumulative evidence</td>
<td>17</td>
<td>Describe how the strength of the body of evidence will be assessed (such as GRADE)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.*

### Search strategy on PubMed

| #1 | "cerebrovascular Disorders"[Mesh] OR "Stroke"[Mesh] |
| #2 | "cerebral Arteries"[MeSH] OR "neurovascular" |
| #3 | #1 OR #2 |
| #4 | transcarotid OR trans-carotid OR carotid OR transcervical OR TCA OR transcarotid artery revascularization OR TCAR |
| #5 | transfemoral" OR "femoral" OR "Femoral Artery"[MeSH] OR trans-femoral OR TFA |
| #6 | #4 AND #5 |
| #7 | #3 and #7 |
Supplement 3. Screening pilot-test form

Level 1 screening

1. Does the study include patients with ischemic and hemorrhagic cerebrovascular diseases?
   YES____ NO____ UNCLEAR____

2. Does the study compare TCA with TFA for cerebrovascular intervention?
   YES____ NO____ UNCLEAR____

3. Is this an RCT, quasi-RCT, prospective, or retrospective case-control study?
   YES____ NO____ UNCLEAR____

If you answer NO to any of these questions, the citation will be excluded. All other citations will be included in L2 screening.

Level 2 screening

1. Does the study include adults (≥18 years old) undergoing cerebrovascular intervention for ischemic and hemorrhagic cerebrovascular diseases?
   YES____ NO____ UNCLEAR____

2. Is this an RCT, quasi-RCT, prospective, or retrospective case-control study comparing TCA with TFA with more than 30 participants of each arm?
   YES____ NO____ UNCLEAR____

3. Does the study report at least one of the following outcomes:
   a. The rates of composite endpoints within 30 days after surgery.
   b. The rates of composite endpoints within 1 year after surgery.
c. Procedural time.

d. Length of hospital stay.

e. Total radiation dose.

f. The rates of death, stroke, MI, cranial nerve injury (CNI), transient ischemic attack (TIA) and other local and systemic complications within 30 days and 1 year after surgery.

YES____ NO____ UNCLEAR____

4. Were the patients undergoing cerebrovascular intervention through transcarotid arterial access?

YES____ NO____ UNCLEAR____

5. Were the patients treated through transcarotid arterial access compared to others through transfemoral arterial access?

YES____ NO____ UNCLEAR____

If you answer NO to any of these questions, the citation/study will be excluded. All other full-text articles will be included.
CODING MANUAL FOR CASE-CONTROL STUDIES

SELECTION

1) Is the Case Definition Adequate?
   a) Requires some independent validation (e.g. >1 person(record/time/process to extract information, or reference to primary record source such as x-rays or medical/hospital records)
   b) Record linkage (e.g. ICD codes in database) or self-report with no reference to primary record
   c) No description

2) Representativeness of the Cases
   a) All eligible cases with outcome of interest over a defined period of time, all cases in a defined catchment area, all cases in a defined hospital or clinic, group of hospitals, health maintenance organisation, or an appropriate sample of those cases (e.g. random sample)
   b) Not satisfying requirements in part (a), or not stated.

3) Selection of Controls
   This item assesses whether the control series used in the study is derived from the same population as the cases and essentially would have been cases had the outcome been present.
   a) Community controls (i.e. same community as cases and would be cases if had outcome)
   b) Hospital controls, within same community as cases (i.e. not another city) but derived from a hospitalised population
   c) No description

4) Definition of Controls
   a) If cases are first occurrence of outcome, then it must explicitly state that controls have no history of this outcome. If cases have new (not necessarily first) occurrence of outcome, then controls with previous occurrences of outcome of interest should not be excluded.
   b) No mention of history of outcome
COMPARABILITY

1) Comparability of Cases and Controls on the Basis of the Design or Analysis

A maximum of 2 stars can be allotted in this category. Either cases and controls must be matched in the design and/or confounders must be adjusted for in the analysis. Statements of no differences between groups or that differences were not statistically significant are not sufficient for establishing comparability. Note: If the odds ratio for the exposure of interest is adjusted for the confounders listed, then the groups will be considered to be comparable on each variable used in the adjustment.

There may be multiple ratings for this item for different categories of exposure (e.g. ever vs. never, current vs. previous or never)

Age = , Other controlled factors = .

EXPOSURE

1) Ascertainment of Exposure

Allocation of stars as per rating sheet

2) Non-Response Rate

Allocation of stars as per rating sheet
CODING MANUAL FOR COHORT STUDIES

SELECTION

1) Representativeness of the Exposed Cohort

Item is assessing the representativeness of exposed individuals in the community, not the representativeness of the sample of women from some general population. For example, subjects derived from groups likely to contain middle class, better educated, health oriented women are likely to be representative of postmenopausal estrogen users while they are not representative of all women (e.g. members of a health maintenance organisation (HMO) will be a representative sample of estrogen users. While the HMO may have an under-representation of ethnic groups, the poor, and poorly educated, these excluded groups are not the predominant users users of estrogen).

Allocation of stars as per rating sheet

2) Selection of the Non-Exposed Cohort

Allocation of stars as per rating sheet

3) Ascertainment of Exposure

Allocation of stars as per rating sheet

4) Demonstration That Outcome of Interest Was Not Present at Start of Study

In the case of mortality studies, outcome of interest is still the presence of a disease/incident, rather than death. That is to say that a statement of no history of disease or incident earns a star.

COMPARABILITY

1) Comparability of Cohorts on the Basis of the Design or Analysis

A maximum of 2 stars can be allotted in this category
Either exposed and non-exposed individuals must be matched in the design and/or confounders must be adjusted for in the analysis. Statements of no differences between groups or that differences were not statistically significant are not sufficient for establishing comparability. Note: If the relative risk for the exposure of interest is adjusted for the confounders listed, then the groups will be considered to be comparable on each variable used in the adjustment.
There may be multiple ratings for this item for different categories of exposure (e.g. ever vs. never, current vs. previous or never)
Age = *, Other controlled factors = *
OUTCOME

1) Assessment of Outcome

For some outcomes (e.g. fractured hip), reference to the medical record is sufficient to satisfy the requirement for confirmation of the fracture. This would not be adequate for vertebral fracture outcomes where reference to x-rays would be required.

a) Independent or blind assessment stated in the paper, or confirmation of the outcome by reference to secure records (x-rays, medical records, etc.)

b) Record linkage (e.g. identified through ICD codes on database records)

c) Self-report (i.e. no reference to original medical records or x-rays to confirm the outcome)

d) No description.

2) Was Follow-Up Long Enough for Outcomes to Occur

An acceptable length of time should be decided before quality assessment begins (e.g. 5 yrs. for exposure to breast implants)

3) Adequacy of Follow Up of Cohorts

This item assesses the follow-up of the exposed and non-exposed cohorts to ensure that losses are not related to either the exposure or the outcome.

Allocation of stars as per rating sheet