First author_____

Title:_____

Journal_____

Year:_____

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Last Page:_____

1. Type of study

❑ Controlled trial without randomization ⇨ Section B
❑ Observational cohort study ⇨ Section B

2. Type of report

❑ Full paper in peer reviewed journal
❑ Full paper in book or other type of report
❑ Abbreviated paper in meeting proceedings or similar publication
❑ Abstract only
❑ Other_____

3. Language

❑ English
❑ Scandinavian
❑ German
❑ French
❑ Other _____

Section B (observational cohort study or controlled clinical trial without randomization)

External validity

Short form answer:

❑ Clear external validity *(0)*
❑ Probable external validity *(1)*
❑ Uncertain external validity *(3)*
❑ External validity cannot be assessed *(5)*

If uncertain, answer questions under Item 1.
Otherwise go to Internal validity (after Item 1)

1. Accrual / selection of study subjects

a. Was the studied exposure well defined (e.g., if follow-up of a specified disease, is the definition of the disease acceptable)?
❑ Yes = 0
❑ No = 2

b. Eligibility / inclusion criteria clearly stated?
❑ Yes = 0
❑ No = 1

c. Consecutive eligible subjects included?
❑ Yes = 0
❑ No = 1
❑ Not stated = 1

d. Numbers and reasons for non-participation given?
❑ Yes = 0
❑ No = 1

e. Exclusion criteria clearly stated and acceptable?
❑ Yes = 0
❑ No = 1

f. Are numbers of excluded persons given by reason (as prescribed in the CONSORT statement)?
❑ Yes = 0
❑ No = 1

Total sum of section 1:
0 = Clear external validity
1 = Probable external validity
2-3 = Uncertain external validity
≥ 4 = External validity cannot be assessed

Internal validity

Short form answer:

- ❑ Excellent internal validity *(0)*
- ❑ Good internal validity *(1)*
- ❑ Acceptable internal validity *(2)*
- ❑ Uncertain internal validity *(4)*
- ❑ Uninformative due to flawed internal validity *(10)*

If uncertain, answer questions under Items 2-6. Otherwise go to Precision (after Item 6)

2. Exposure assessment

a. Was the studied exposure satisfactorily measured / recorded?
- ❑ Yes = 0
- ❑ Yes, with minor criticism = 1
- ❑ No = 3

b. Were *all* in the exposed group really exposed?
- ❑ Yes = 0
- ❑ Yes, probably = 1
- ❑ No, probably not = 2
- ❑ No = 2

c. Were *all* in the reference category really unexposed?
- ❑ Yes = 0
- ❑ Yes, probably = 1
- ❑ No, probably not = 2
- ❑ No = 2

3. Comparability of groups / selection bias / confounding

   a. Was there an account of the comparability of groups with regard to factors that might conceivably affect the outcome (potential confounding factors)? *(If only one cohort was studied and compared with the background population or historical controls – was there data to support the comparability with the reference category).*

❑ Yes = 0
❑ No = 3

   b. Did the investigators consider all <u>important</u> potential confounding factors (*potential confounding factors = factors that are independent causes of / risk factors for / protective factors against the outcome, AND not a link in the causal chain between the studied exposure and the outcome*)?

❑ Yes = 0
❑ Probably = 1
❑ No = 3
❑ No data given = 0 (already scored under 3a)

   c. Were the relevant confounding factors satisfactorily measured / recorded?

❑ Yes = 0
❑ Yes, with minor criticism = 1
❑ No = 3

   d. Were the potential confounding factors unevenly distributed among exposed and /non-exposed/ reference group (*confounding arises if factors described under 3b are unevenly distributed among exposed and unexposed [i.e., linked to the exposure]*)?

❑ Yes = 2
❑ No = 0
❑ No data given = 0 (already scored under 3a)

   e. Were attempts in the analysis to adjust for imbalances between exposure groups with regard to potential confounding factors (e.g., through restriction, stratified analyses, or multivariate modelling)?

❑ Not needed (no important imbalances) = 0
❑ Yes = -2 (subtract 2 if you scored 2 under 3d)
❑ No, despite a need = 2

4. Evaluation of outcome, ascertainment / detection bias

   a. Was there an acceptable definition of the outcome?

❑ Yes = 0
❑ No = 3

   b. Was the outcome clinically relevant?

❑ Yes = 0
❑ Of questionable relevance = 2
❑ Irrelevant ➔ **study is deemed uninformative, excluded**

c. Were the evaluators of the outcome aware of exposure status of the cohort members?

❑ Yes = 1
❑ Probably = 1
❑ No = 0

d. Was there any reason to believe that there was important ascertainment / detection bias (*e.g., exposure linked to smoking, and smoking, in turn, linked to higher frequency of health care visits, and thus a more intense surveillance*)?

❑ Yes = 2
❑ No = 0

5. Losses to follow-up

a. Was there an account of the numbers of subjects who were lost to follow-up?

❑ Yes = 0
❑ No = 3

b. What proportion was lost to follow-up?

❑ <10% = 0
❑ 10-19% = 1
❑ 20-29% = 2
❑ 30-39 = 3
❑ ≥ 40% ➔ **study is deemed uninformative, excluded**
❑ Proportion not stated = 0 (scored under 5a)

6. Analysis

a. Was the main outcome variable defined in advance and was the conclusion of the study based on the analysis of this variable?

❑ Yes = 0
❑ No (or not mentioned in the report) = 1

b. Was there a prior hypothesis?

❑ Yes = 0
❑ No (or not mentioned in the report) = 1

c. Was the statistical method adequate?

❑ Yes = 0
❑ No = 3

<u>Total sum of Items 2-6 (internal validity)</u>:
0-1= Excellent internal validity
2-3 = Good internal validity
4-6 = Acceptable internal validity
7-9 = Uncertain internal validity
≥ 10 = Uninformative due to flawed internal validity

Precision

Short form answer:

❑ Premeditated and sufficient study size *(0)*
❑ Sample size of uncertain adequacy *(2)*
❑ Probably underpowered study *(4)*

If uncertain, answer questions under Items 7-8

7. Smallest clinically relevant effect

   a. Was the smallest clinically relevant effect defined?
   ❑ Yes = 0
   ❑ No = 1

   b. Was the stated smallest clinically relevant effect reasonable?
   ❑ Yes = 0
   ❑ No = 1
   ❑ Not defined = 0 (scored under 10a)

8. Study power

   a. Were the deliberations behind the sample size decision clearly described?
   ❑ Yes = 0
   ❑ No = 2

   b. What was the power to detect a reasonably-sized smallest clinically relevant effect?
   ❑ Not stated because there was a strong and statistically significant effect = 0
   ❑ ≥ 90% = 0
   ❑ 80-89% = 1
   ❑ 70-79% = 2
   ❑ <70% = 3
   ❑ Not stated despite a non-significant finding = 4

Total sum of Items 7-8 (precision)
0-1 = Premeditated and sufficient study size
2-3 = Sample size of uncertain adequacy
≥ 4 = Probably underpowered study