Tool for assessing risk of bias- Newcastle-Ottawa Scale modified

1- Selection Bias – Is the source population (cases, controls, cohorts) appropriate and representative of the population of interested? (Methods for selection study participants).

1 (low risk of bias)

The investigators describe a:

- random selection from a population that is representative of the condition under study
- A consecutive sample from a population that is representative of the condition under study
- Eligible, exposed individuals from a defined population

Quote: “ ”

2 (moderate risk of bias)

- A consecutive sample from a population that is not highly representative of the outcome of interest
- A random selection from a population that is not highly representative of the outcome of interest

Quote: “ ”

3 (high risk of bias)

Non-random approach, for example:

- The source population cannot be defined or enumerated
- Volunteering or self-recruitment
- No description of the derivation of the cohort

Quote: “ ”

? (unclear risk of bias)

- Insufficient information to permit judgment of ‘1’, ‘2’ or ‘3’
### 2- Performance Bias (Methods to control for confounding)

#### 2.1. Is the sample size sufficient and is there sufficient power to detect a meaningful difference in the outcome of interest?

1. **Low risk of bias**
   - Sample size was adequate and there was sufficient power to detect a difference in the outcome
   - Quote: “

2. **Moderate risk of bias**
   - Sample size may not be adequate and study may have been slightly underpowered
   - Quote: “

3. **High risk of bias**
   - Sample size was small and there was not enough power to test the outcome of interest
   - Quote: “

? **Unclear risk of bias**
   - Insufficient information to permit judgment of ‘1’, ‘2’ or ‘3’

#### 2.2. Did the study adjust for any variables or confounders that may influence the outcome?

1. **Low risk of bias**
   - The study identified and adjusted for all possible confounders that may influence the estimates of association between exposure and outcome
   - Quote: “

2. **Moderate risk of bias**
   - The study identified and reported possible variables that may influence the outcome but did not statistically explore their influence
   - Quote: “

3. **High risk of bias**
   - The study either did not report any variables of influence or acknowledge any variables of influence when it was clear they were present.
3- Detection bias (Statistical methods)

3.1. Did the study use appropriate statistical analysis methods relative to the outcome of interest?

1 (low risk of bias) □

Any one of the following:

• The study reported use of appropriate statistical analysis as required □

   □ Quote: “”

2 (moderate risk of bias) □

• The study used either correct statistical methods but did not report them well, or used the incorrect methods but reported them in detail □

   □ Quote: “”

3 (high risk of bias) □

• The study did not use appropriate statistical analysis as required □

   □ Quote: “”

? (unclear risk of bias) □

• Insufficient information to permit judgment of ‘1’, ‘2’ or ‘3’ □

3.2. Is there little missing data and did the study handle it accordingly?

1 (low risk of bias) □

• The study acknowledged missing data to be less than 10% and specified the method of handling it □

• No missing data □

   □ Quote: “”
2 (moderate risk of bias) □

- The study either had greater than 15% of missing data but they specified the method used to handle it □
- Missing data is not excessive, and they specified the method used to handle it □
  □ Quote: “”

3 (high risk of bias) □

- The study had greater than 15% of missing data and did not handle it at all □
  □ Quote: “”

? (unclear risk of bias) □

- Insufficient information to permit judgment of ‘1’, ‘2’ or ‘3’ □

4- Information bias (Methods of measuring outcome variables)

4.1. Is the methodology of the outcome measurement explicitly stated and is it appropriate?

1 (low risk of bias) □

- The study provides a detailed description of the outcome measure(s) which are appropriate for the outcome of interest □
  □ Quote: “”

2 (moderate risk of bias) □

- The study provides a somewhat complete description of outcome measurements that are justified □
  □ Quote: “”

3 (high risk of bias) □

- The study provides limited information on the methods of measuring the outcome and the measure is not appropriate considering the outcome □
  □ Quote: “”
4.2. Is there an objective assessment of the outcome of interest?

1 (low risk of bias)
- The study used objective methods to discern the outcome status of participants (i.e. laboratory measurements, medical records)
- Quote: ""

2 (moderate risk of bias)
- The study relied on subjective data as the primary method to discern the outcome status of participants (i.e. self-report)
- Quote: ""

3 (high risk of bias)
- The study had limited reporting about assessment of outcomes
- No description
- Quote: ""

? (unclear risk of bias)
- Insufficient information to permit judgment of ‘1’, ‘2’ or ‘3’

5- Attrition bias (Subject follow-up)

5.1. Was the follow-up sufficiently long enough for the outcome to occur?

1 (low risk of bias)
- Follow-up was sufficiently long enough for the outcome to occur
- Quote: ""

3 (high risk of bias)
- Follow-up was not sufficiently long enough for the outcome to occur
- Quote: ""
5.2. Was there minimal loss to follow-up and are subjects lost to follow-up unlikely to introduce bias?

1 (low risk of bias)

- Follow-up was completed for all, or nearly all subjects, and reasons for losses to follow-up were well documented.
  
- Quote: ""

2 (moderate risk of bias)

- Losses to follow-up are not excessive, and reasons for losses to follow-up are well documented and mostly unrelated to the outcome
  
- Quote: ""

3 (high risk of bias)

- Significant loss to follow-up, reasons for losses to follow-up not reported, suspect that reasons for dropouts are related to the outcome
  
- Quote: ""

? (unclear risk of bias)

- Insufficient information to permit judgment of ‘1’ or ‘3’